JAN 29 1959

Next Meeting, The American Association for Thoracic Surgery, Los Angeles, California, April 21, 22, and 23, 1959, Headquarters, Hotel Statler

VOLUME 37
NUMBER 1
JANUARY, 1959

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The Journal of Thoracic Surgery

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Official Organ

The American Association for Thoracic Surgery

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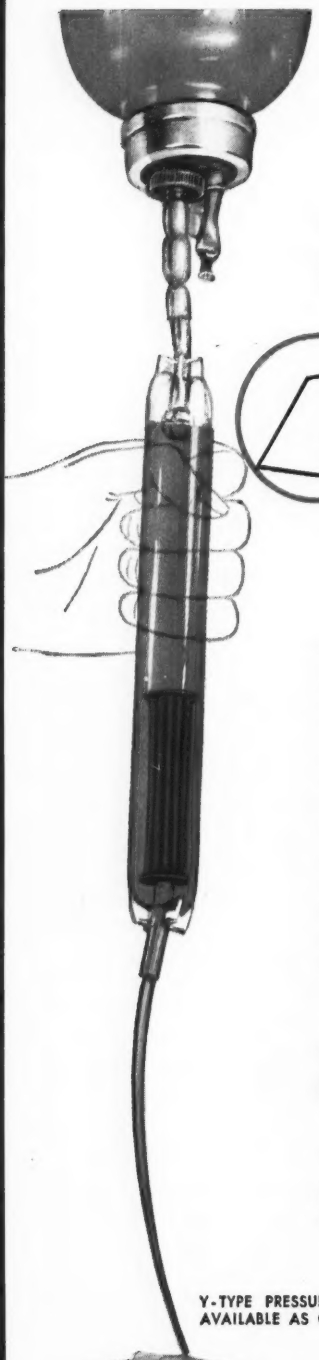

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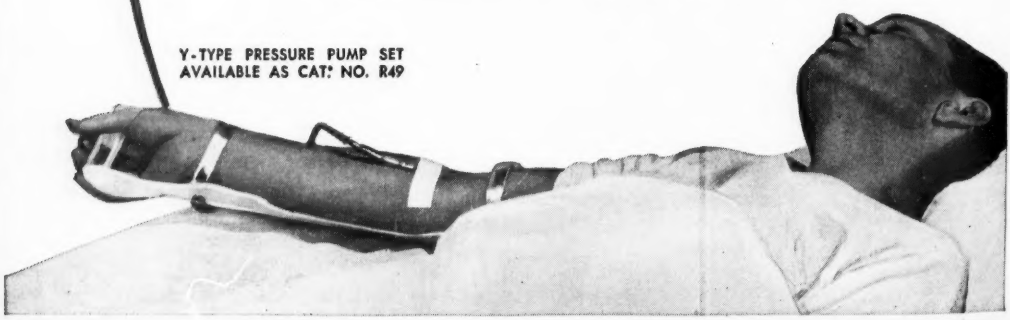

The Journal of Thoracic Surgery

VOLUME 37
JANUARY 1959
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Original Communications

CREATION OF A TEMPORARY ARTIFICIAL DUCTUS FOR THE SURGICAL CORRECTION OF VENTRICULAR SEPTAL DEFECTS ASSOCIATED WITH SEVERE PULMONARY HYPERTENSION

A Two-Stage Operation

Howard D. Sirak, M.D. (by invitation), and Don M. Hosier, M.D. (by invitation), Columbus, Ohio

WHEN an interventricular septal defect is associated with severe pulmonary hypertension, surgical correction has resulted in a high operative mortality. In Lillihei's series of patients over 2 years of age in whom the pulmonary artery systolic pressure was 70 per cent or more of the aortic systolic pressure, the operative mortality has been reported as 37 per cent.[1] In those cases, in which the pressures in the two systems are essentially equal, the mortality has been even greater.[2, 3, 4] However, it will be recalled that most young children with an atypical ductus and equal-pressure pulmonary hypertension have tolerated surgical closure.[5, 6] A possible explanation for this difference in results is that, in the case of interventriculer septal defect, the cardiovascular system cannot withstand the combined burdens of open-heart surgery and those imposed by the physiologic readjustment to defect closure. Therefore, it seemed worth while to try to lower operative mortality by preventing these two major burdens

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Supported by grants from the Central Ohio Heart Association and the Bremer Foundation.

Read at the Thirty-eighth Annual Meeting of The American Association for Thoracic Surgery at Boston, Mass., May 16-18, 1958.

from coinciding in one operation. Accordingly, a two-stage operation was devised for those children with ventricular septal defects in whom the systolic pressures in the pulmonary artery and aorta were essentially equal. The first stage consists of establishing a temporary ductus between the ascending aorta and the pulmonary artery and closing the interventricular septal defect. At the second stage, performed 3 to 6 months later, after the heart and lungs have recovered from the operative manipulation, the artificial ductus is divided. In this manner, the final correction, which imposes the severest physiologic burden, is accomplished by a lesser operative undertaking.

OPERATIVE PROCEDURE

The patient is prepared for open-heart surgery* in the usual fashion: He is placed on the table in the supine position, both common femoral arteries are isolated between umbilical tapes, and the chest opened bilaterally via a transverse transsternal incision through the fourth interspace. The pericardium is incised transversely and then parallel to the right phrenic nerve and retracted with the sternum. The ascending aorta is dissected free and encircled with an umbilical tape. The superior (central to the azygos vein) and inferior venae cavae are doubly encircled with siliconed umbilical tapes.

The First Stage.—At a site about 1½ to 2 cm. from the base of the aorta, its anteromedial surface is cleaned of adventitia as is a corresponding area on the right anterolateral aspect of the main pulmonary artery. A portion of the aortic—and then the pulmonary artery—lumen is isolated for anastomosis by means of a curved vascular clamp. An elliptical piece of tissue is removed from each vessel wall; otherwise, if the anastomosis is done to a longitudinal slit, thrombosis of the graft is prone to occur. A graft, with an inside diameter of approximately 10 mm., is then anastomosed in end-to-side fashion employing a continuous 5-0 arterial silk (Fig. 1). The aortic clamp is left in place until the pulmonary artery anastomosis is completed. To prevent kinking of the graft, both ends should be cut obliquely.

Several types of graft materials have been employed. Nylon grafts (Edwards-Tapp) have been tried, but are no longer used because hemostasis at the suture lines may become troublesome after the patient is heparinized and, more important, the ends cannot be conveniently tailored inside the chest. Aortic homografts were found to be most suitable at the time of the first stage, but imposed a difficult technical problem at the second stage because more operative exposure was needed to permit placing the sutures directly in the walls of the aorta and pulmonary artery. It would be inadvisable simply to close the divided ends of the homograft lest future rupture occur. Both of these requirements can be met by putting a 1.5 cm. sleeve of seamless Dacron cloth tubing† over each end of a child's aortic homograft of appropriate diameter and incorporating it in the anastomosis.

*Kay-Cross Oxygenator, manufactured by Pemco, Inc., Cleveland.

†Available from John B. Sidebotham, Inc., 4317 Griscom Street, Frankford, Philadelphia 24, Pa.

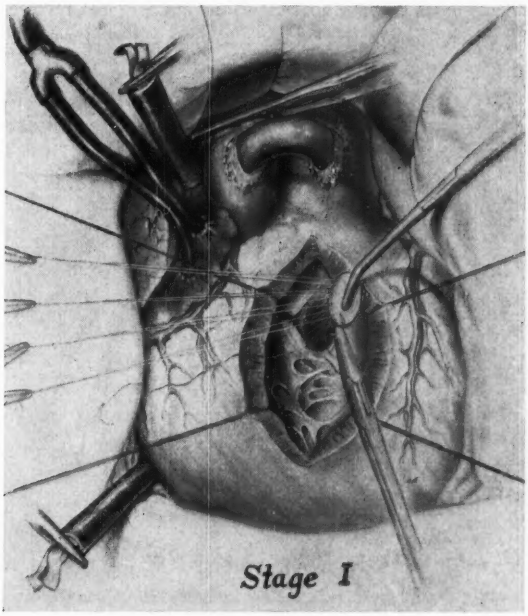

Fig. 1.—Stage One. Open-heart procedure. The artificial "ductus" is placed between the ascending aorta and main pulmonary artery. The septal defect is closed employing potassium citrate arrest.

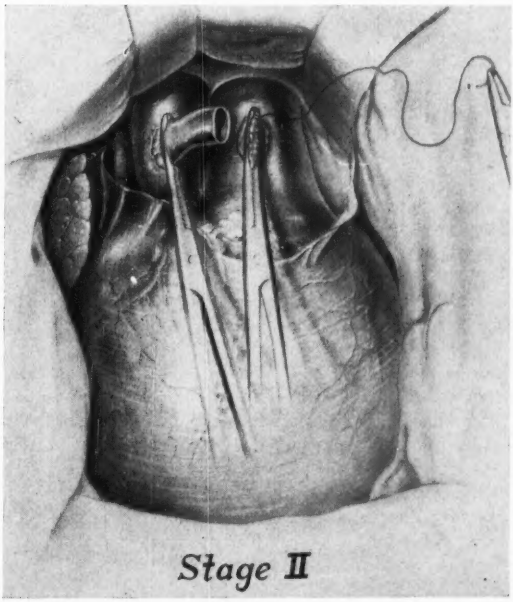

Fig. 2.—Stage Two. Three to 6 months later, the temporary "ductus" is divided and oversewn close to each great vessel.

Upon completing both anastomoses, the pulmonary artery clamp is removed, gradually at first, until the suture lines cease leaking. The aortic clamp is then removed. After the operator is satisfied with the hemostasis, the patient is heparinized (3 mg./Kg. body weight) and then cannulated for the extracorporeal bypass. During the bypass, the graft is occluded with a bulldog clamp. Elective cardiac arrest, with the aorta cross-clamped distal to the graft site, is used during the repair of the defect. If the defect is large (over 1 cm.), a double-thickness Teflon cloth* patch is sewn in place employing mattress sutures of atraumatic 3-0 Dacron.† If it is smaller, the sutures are passed through and tied over a cigarette-shaped pledget of Ivalon sponge. The aortic clamp is removed and, when adequate heart action has returned, the ventricular incision is repaired. The bulldog clamp on the graft is removed after the vena caval tourniquets have been loosened and the pump-oxygenator perfusion rate has been cut back to about 30 per cent of its original level. The patient is decannulated and protamine is injected. The anastomoses are again inspected for hemostasis, after which the pericardium is loosely closed over the graft.

Stage II.—The child is placed in the supine position with the right side elevated about 30 degrees. The right-sided portion of the previous skin incision is excised and the chest entered through the third interspace. The adherent lung and pericardium are dissected away from the mediastinum in the area of the graft which can now be palpated. The graft is cross-clamped, divided, and closed with sutures. The suturing is placed as close to each great vessel as possible incorporating both the homograft and the Dacron cloth sleeve (Fig. 2).

CASE REPORTS

CASE 1.—D. L., a 3-year-old boy who previously had had multiple operations for other congenital defects including pyloric stenosis, cleft palate, and inguinal hernia, was admitted for evaluation of a heart murmur that had been recognized since birth. His parents stated that he had repeated respiratory infections and his exercise tolerance was limited.

The child placed below the third percentile on the growth chart. On auscultation a Grade 2 (1-4) systolic murmur was heard along the left sternal border, being loudest in the third left intercostal space near the sternum. This murmur was not widely transmitted. P_2 was loud and snapping and a faint short diastolic murmur was present in the pulmonic area.

The electrocardiograph showed right and left ventricular enlargement (Fig. 3). The teleoroentgenogram demonstrated cardiac enlargement and increased pulmonary vascular markings (Fig. 4). On fluoroscopy, the activity of the pulmonary arteries was found to be moderately increased over normal. Cardiac catheterization done on Jan. 29, 1957, under morphine and Nembutal sedation, disclosed equal pressures in the greater and lesser circulations (Table I). The catheter passed through a ductus into the aorta. The next day blood samples were obtained simultaneously from the right brachial and femoral arteries. A differential in saturation of the samples was noted (Table I). A diagnosis was made of interventricular septal defect and patent ductus arteriosus with equal-pressure pulmonary hypertension and predominant left-to-right shunt at the septal defect with some reversal of flow through the ductus. The child was discharged to await scheduling for open-heart surgery.

The child was readmitted for the first part of a two-stage operation. On May 17, 1957, the ductus, which was very short and about 5 mm. in diameter, was first isolated and temporarily occluded with an umbilical tape. The patient was then cannulated for extracorporeal bypass. The interventricular septal defect was 12 mm. in diameter and, employing

*Available from John V. Sidebotham, Inc., 4317 Griscom Street, Frankford, Philadelphia 24, Pa.

†Supplied by Mr. C. W. Norman, Ethicon, Inc., Somerville, N. J.

potassium citrate arrest, a double-thickness patch of Teflon cloth was sewn in place, using interrupted mattress sutures of 3-0 atraumatic Dacron. As the bypass was being discontinued, the tourniquet on the ductus was released. During the early postoperative period, difficulty with secretions necessitated a tracheotomy.

This patient was again admitted approximately 6 months later. He had gained weight and his color had improved. A systolic murmur could be heard over the left second interspace. The electrocardiograph showed some regression of the right ventricular hypertrophy pattern.

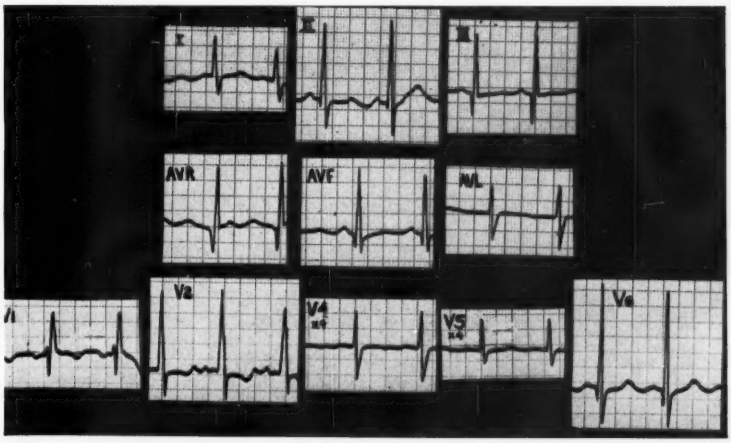

Fig. 3.—Case 1. Preoperative electrocardiograph showing an incomplete right bundle branch block with a tall R wave in aV_R indicating right ventricular hypertrophy. The tall R wave in V_5 and V_6 is evidence of left ventricular hypertrophy. (Paper speed, 50 mm./sec.)

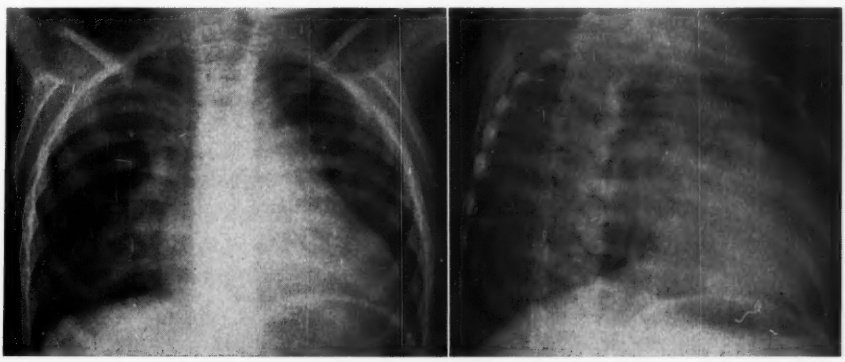

Fig. 4.—Case 1. Chest roentgenograms (PA and RAO) demonstrating cardiac enlargement, prominent pulmonary conus, and accentuated hilar vascular markings.

On fluoroscopy, the hilar activity still appeared to be accentuated. An attempt at catheterization was unsuccessful. On Dec. 18, 1957, through a left posterolateral incision, the ductus was redissected and divided. The patient made an uneventful recovery.

The child was readmitted to the hospital on Feb. 20, 1958, 3 months after the second stage for cardiac catheterization. The data showed a marked regression in pressures and normal saturation values (Table I).

Comment: The fact that the pressures had returned to the upper limits of normal (with the patient sedated) just 3 months after the second stage tends to corroborate the large

role played by the flow-factor in this patient. It would be reasonable to assume that the vascular changes present in the lung (Fig. 5) certainly could not have had time to regress completely; thus, one might infer that there was still a reduction in wall:lumen ration, but that ample capacity remained once the excess flow was removed. Therefore, the "temporary"

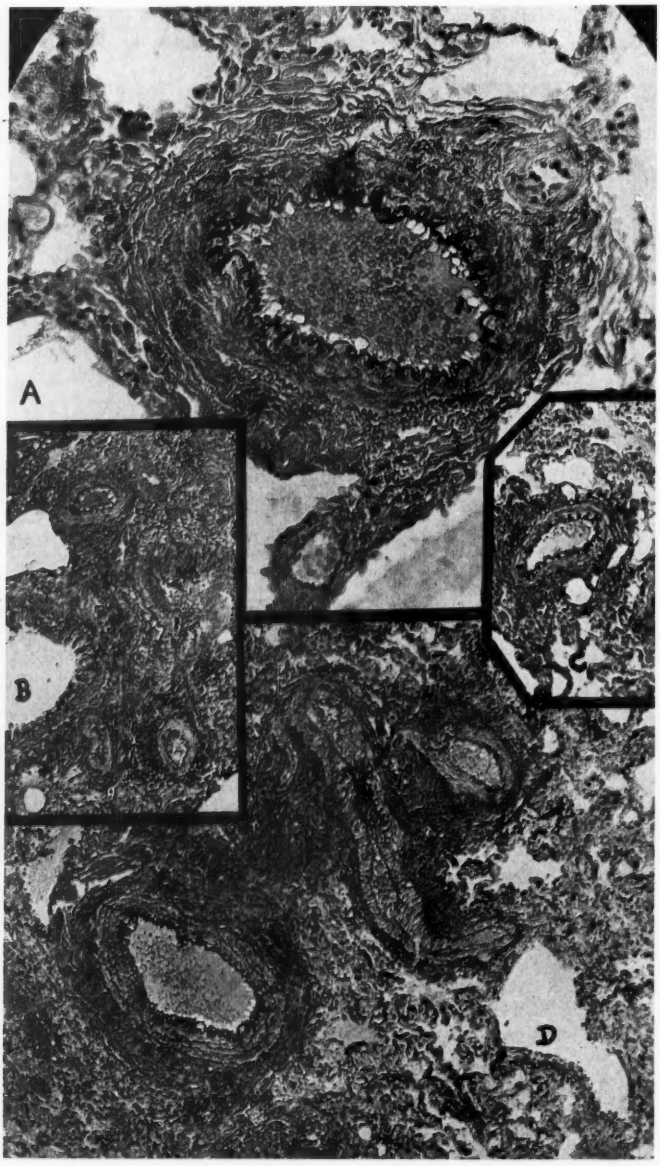

Fig. 5.—Case 1. Photomicrograph of the lung biopsy obtained at the first stage showing moderately severe changes in the small muscular arteries. *A*, × 225; *B*, *C*, and *D*, × 100.

ductus may have aided the immediate postoperative recovery from the open-heart surgery by compensating for the effects of a possible superimposed functional pulmonary vascular component. The latter might be initiated by the alteration of the pulmonary blood flow and the manipulation of the heart and lungs.

TABLE I

D. L.	PREOPERATIVE		AFTER CLOSURE OF DUCTUS	
	SATURATION PER CENT	PRESSURE (MM. HG)	SATURATION PER CENT	PRESSURE (MM. HG)
Superior vena cava	66.5		69.5	
Right atrium	68	7	70	4
Right ventricle	83	80/0	69	35/0
Pulmonary artery	83.5	80/35	70.5	34/9
Aorta	93	80/46		
Right femoral artery	90*		90	64/36
Right brachial artery	98*			

Case 1. Cardiac catheterization data obtained before the first stage demonstrated an interventricular septal defect and a patent ductus arteriosus with equal-pressure pulmonary hypertension. There is a 15 per cent step-up in saturation of the right ventricular sample. The catheter passed through the patent ductus into the aorta. Simultaneous samplings of the right brachial and femoral arteries indicated flow reversal through the ductus. Two months after the second stage, on repeat catheterization, the saturations had returned to normal, and the pulmonary artery pressures had regressed toward normal. The low systemic arterial pressure suggests that the pulmonary artery pressure may actually be higher than the figures indicate.

*Simultaneous preoperative studies done without sedation.

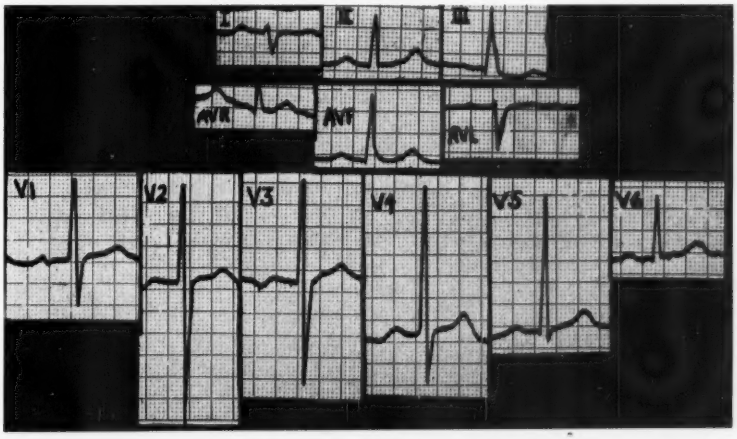

Fig. 6.—Case 2. Preoperative electrocardiogram showing right ventricular hypertrophy. The tall R wave in V_5 suggests some left ventricular hypertrophy. (Paper speed, 50 mm./sec.)

CASE 2.—D. K., a 4½-year-old girl, was referred for correction of a cleft palate. On examination, a heart murmur was detected, and a cardiac consultation was obtained. The child placed below the third percentile on the growth chart. There was a slight left precordial bulge and a faint thrill could be palpated over the third and fourth intercostal spaces. A coarse Grade 2 (1-4) systolic murmur was present along the left sternal border, being maximal in the fourth left intercostal space near the sternum. P_2 was markedly accentuated.

The electrocardiograph showed evidence of both right and left ventricular hypertrophy (Fig. 6). A teleoroentgenogram (Fig. 7) demonstrated enlargement of the heart with increased pulmonary vascular markings. On fluoroscopy, pulsations of the pulmonary arteries

were considered to be moderately increased over normal. Cardiac catheterization was performed (Table II) and a diagnosis was made of interventricular septal defect with equal-pressure pulmonary hypertension with significant left-to-right shunt.

The child was discharged and readmitted at a later date. On July 17, 1957, the first-stage operation was undertaken. Exclusion clamps were placed on the ascending aorta and pulmonary artery, the wall of each was incised longitudinally, and a nylon graft (Edwards-Tapp), 3/16 inch inside diameter, was sewn in place. After the bypass was established, a 15 mm. septal defect was closed employing a double-thickness Teflon cloth patch. When the bypass was discontinued, the patient's heart seemed incapable of maintaining an adequate

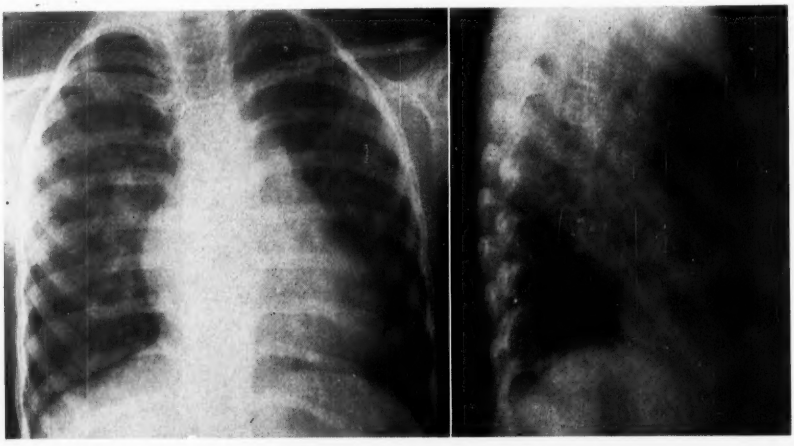

Fig. 7.—Case 2. PA and right lateral chest roentgenograms showing cardiac enlargement and prominent hilar vascular markings.

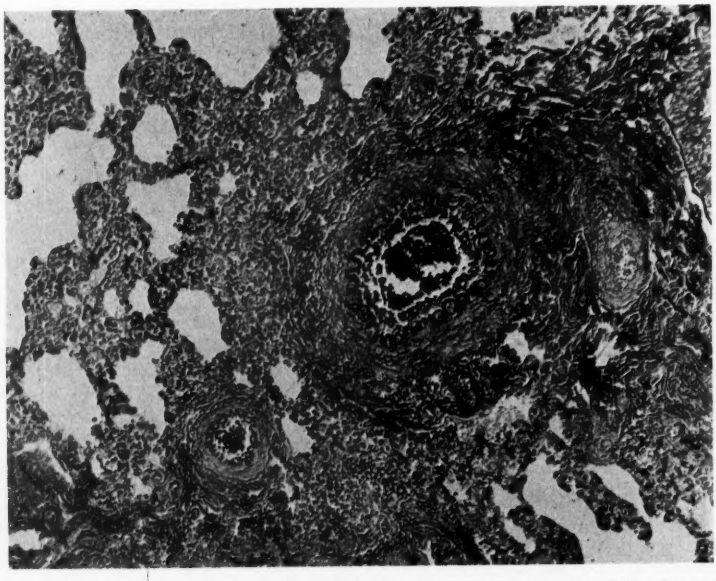

Fig. 8.—Case 2. Photomicrograph of tissue obtained from a central area of the lung showing moderately severe medial hypertrophy of the small muscular arteries. (× 90.)

TABLE II

D. K.	PREOPERATIVE	
	SATURATION PER CENT	PRESSURE (MM. HG)
Inferior vena cava	78	
Right atrium	76	7
Right ventricle	86	84/0
Pulmonary artery	88	86/35
Femoral artery	96	90/60

Case 2. Preoperative catheterization diagnostic of interventricular septal defect with equal-pressure pulmonary hypertension. There is about a 10 per cent step-up in the right ventricular sample.

circulation. A thrill could not be palpated in the main pulmonary artery opposite the anastomosis. The child's condition remained precarious and she died 30 minutes after completion of the chest closure.

Comment: The graft employed in this patient was much too small and the anastomoses were not satisfactory, having been done to longitudinal incisions in the aorta and pulmonary artery. It is believed that due to these two technical errors there was probably no flow across the graft and, therefore, it did not fulfill its intended function. The adverse behavior of the child's circulatory system, commencing shortly after the pump was turned off, is characteristic of this group of patients.

The photomicrograph of lung tissue obtained at autopsy demonstrates moderately severe vascular changes (Fig. 8).

CASE 3.—M. F., a small 5-year-old girl, was admitted for evaluation of a heart murmur. A systolic thrill was palpable along the left sternal border. A harsh, blowing Grade 3 (1-4) systolic murmur could be heard along the left sternal border. Although it was maximal in the fourth left intercostal space near the sternum, it was transmitted over the entire precordium. P_2 was markedly accentuated.

An electrocardiograph (Fig. 9) demonstrated an incomplete right bundle branch block with evidence of both right and left ventricular hypertrophy. Teleoroentgenograms (Fig. 10) showed an enlarged heart with an increase in the pulmonary vascular markings. On fluoroscopy, the pulsatile activity of the pulmonary arteries appeared to be moderately increased. Cardiac catheterization was performed and a diagnosis of interventricular septal defect with equal-pressure pulmonary hyptertension and significant left-to-right shunt was made (Table III).

TABLE III

M. F.	PREOPERATIVE		AFTER CLOSURE OF DUCTUS	
	SATURATION PER CENT	PRESSURE (MM. HG)	SATURATION PER CENT	PRESSURE (MM. HG)
Inferior vena cava				
Right atrium	69	6	72	3.5
Right ventricle	74	82/0	68.5	26/0
Pulmonary artery	76	80/34	66	24/7
Femoral artery	85	86/40	100	94/56

Case 3. The preoperative catheterization demonstrates an interventricular septal defect with equal-pressure pulmonary hypertension. There is about a 5 per cent step-up in the right ventricular sample. The desaturation of the femoral sample may have been influenced by sedation. Recatheterization 6 months later shows a return to normal hemodynamics.

The patient was readmitted at a later date for the first of the two-stage procedure. A ⅜ inch, inside diameter, Edwards-Tapp graft was placed between the ascending aorta and the pulmonary artery. An elliptical piece of vessel wall was removed at each anastomotic site. The bypass was then established and an 8 mm. septal defect was closed with three 3-0 atraumatic Dacron sutures. After the bypass was discontinued, a strong thrill could be palpated in the pulmonary artery opposite the "ductus." A tracheotomy was performed.

The child made an uneventful recovery. A systolic shunt murmur could be heard over the upper portion of the sternum until the tenth postoperative day when it disappeared. It was suspected that the graft had become clotted. The child continued to do well and was discharged home on the fourteenth postoperative day after the tracheotomy wound had healed.

This patient was again admitted in January, 1958, 6 months following the surgery, for recatheterization. The shunt murmur was still absent. The data showed that the saturations and pressures had returned to normal (Table III).

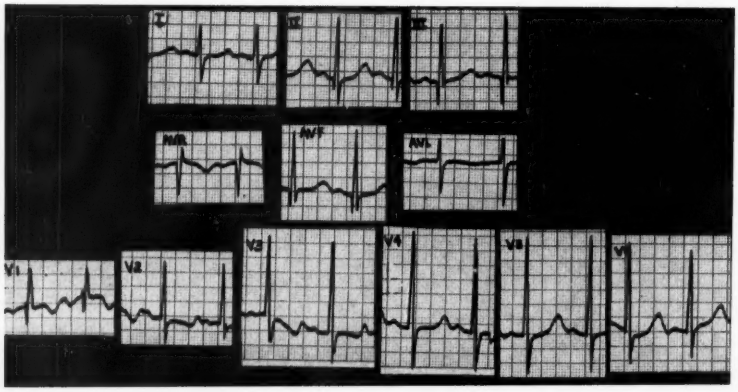

Fig. 9.—Case 3. Preoperative electrocardiograph showing an incomplete right bundle branch block with evidence of enlargement of both ventricles. (Paper speed, 50 mm./sec.)

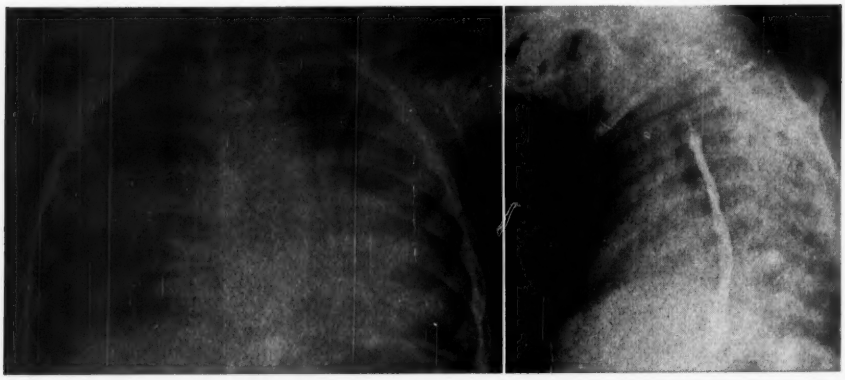

Fig. 10.—Case 3. PA and LAO chest roentgenograms showing cardiac enlargement and accentuated hilar vascular markings. The film was taken during expiration which exaggerates the transverse diameter of the heart.

Comment: The step-up of only 6 per cent in the preoperative right ventricular catheterization sample points to a rather small shunt across the defect; perhaps this explains why the graft ultimately became clotted. This was confirmed by recatheterization. It was very gratifying to note that the pressures and saturations in the right ventricle and pulmonary artery had all returned to normal values. The smooth postoperative course in this patient suggests that the shunt-graft may be needed only during the very early postoperative period and that, after this time, there is adequate recovery from the ventricular incision and the bilateral thoracotomy so that its function was no longer necessary. On the other hand, it may mean that this was one patient who would have tolerated a one-stage correction. However, we were unable to discover anything different in the clinical findings or laboratory data which would have helped us preoperatively to distinguish it from the other cases of its kind.

CASE 4.—N. W., a 5-year-old girl, was admitted for evaluation of a heart murmur. The child was below the third percentile on the growth chart. A systolic thrill was palpated over the third and fourth left intercostal spaces near the sternum. A harsh, blowing Grade 3 (1-4) systolic murmur was heard loudest in the same area and was transmitted over the entire left chest. P_2 was loud and snapping.

An electrocardiograph (Fig. 11) showed an incomplete right bundle branch block with evidence of both right and left ventricular hypertrophy. A teleoroentgenogram (Fig. 12) demonstrated an enlarged heart and accentuated pulmonary vascularity. On fluoroscopy, the activity of the pulmonary arteries was found to be moderately increased. Cardiac cateterization was performed (Table IV). A diagnosis of ventricular septal defect with equal-pressure pulmonary hypertension and significant left-to-right shunt was made.

TABLE IV

	PREOPERATIVE	
N. W.	SATURATION PER CENT	PRESSURE (MM. HG)
Superior vena cava	70	
Right atrium	69	7
Right ventricle	76	82/0
Pulmonary artery	78	85/40
Femoral artery	85	90/50

Case 4. Preoperative catheterization studies were diagnostic of an interventricular septal defect with equal-pressure pulmonary hypertension. There was an 8 per cent step-up in the right ventricular sample. The desaturation of the femoral artery sample may be due to sedation.

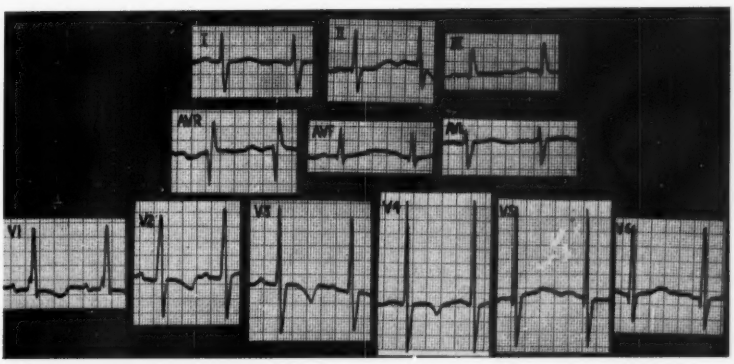

Fig. 11.—Case 4. Preoperative electrocardiograph showing right ventricular hypertrophy and evidence of some left ventricular enlargement. (Paper speed, 50 mm./sec.)

On Aug. 7, 1957, the child was readmitted for the first stage of the two-stage operation. A homograft, 10 mm. in inside diameter, was inserted between the aorta and the pulmonary artery. An elliptical piece of vessel wall was removed from each great vessel. Each end of the graft was cut obliquely. The bypass was instituted and an 8 mm. septal defect was repaired with several atraumatic 3-0 Dacron sutures. A tracheostomy was performed. The patient made an uneventful convalescence. Postoperatively, a loud systolic murmur could be heard over the upper end of the sternum.

The child was readmitted 3 months later for the second-stage operation. The loud shunt murmur was still present over the upper end of the sternum. The right chest was reopened through a portion of the previous incision. The lung and pericardium were dissected away from the area of the temporary "ductus." Because a homograft had been employed, it was deemed necessary, after dividing the shunt, to place the sutures directly in the wall of the

pulmonary artery and aorta. In order to gain adequate exposure of the pulmonary anastomotic site, the sternum had to be transected, but the left pleural space was not entered. The child made an uneventful recovery.

Comment: The postoperative course of this patient following the first stage was strikingly smooth. This supported our belief in the importance of employing a large diameter graft in order to be assured of sustaining an ample left-to-right shunt. Her recovery from the second stage was similarly uneventful. She will be recatheterized again at a later date.

Fig. 12.—Case 4. PA and right lateral chest roentgenograms showing cardiac enlargement and accentuated hilar vascular markings.

CASE 5.—J. S., an 11-year-old boy, who had previously been treated for a brain abscess, was readmitted for evaluation of a heart murmur noted during the first admission. The parents reported that he readily became tired on exertion and that at times his lips became blue.

A soft, Grade 1 (1-4) systolic murmur could best be heard in the fourth left intercostal space near the sternum. P_2 was very loud and snapping.

The hemoglobin was 15.7 grams. The electrocardiogram (Fig. 13) showed only a right ventricular hypertrophy pattern. A teleoroentgenogram demonstrated the heart size to be within normal limits with an increased prominence of the pulmonary conus and pulmonary arteries extending to about the mid-lung area (Fig. 14). However, the peripheral vascular markings were not considered to be increased over normal. On fluoroscopy, the pulsations of the pulmonary arteries were demonstrated to be only minimally increased over normal. Cardiac catheterization was performed (Table V). A diagnosis was made of interventricular septal defect with equal-pressure pulmonary hypertension with minimal left-to-right shunting and beginning reversal of flow.

TABLE V

	PREOPERATIVE	
J. S.	SATURATION PER CENT	PRESSURE (MM. HG)
Superior vena cava	78	
Right atrium	79	6
Right ventricle	82	82/0
Main pulmonary artery	84	84/40
Brachial artery	92	86/56

Case 5. Preoperative catheterization studies indicating a small left-to-right shunt at the ventricular level and equal-pressure pulmonary hypertension. This was not increased by the inhalation of oxygen. The peripheral arterial sample (when coupled with other data) may indicate early flow-reversal because the patient was not sedated.

It was recognized that the vascular changes in this patient were much more marked than in any of the previous patients. The parents were apprised of our grave forebodings, but they wished the child to be given every opportunity. Accordingly, the child was discharged to be scheduled for open-heart surgery at a later date.

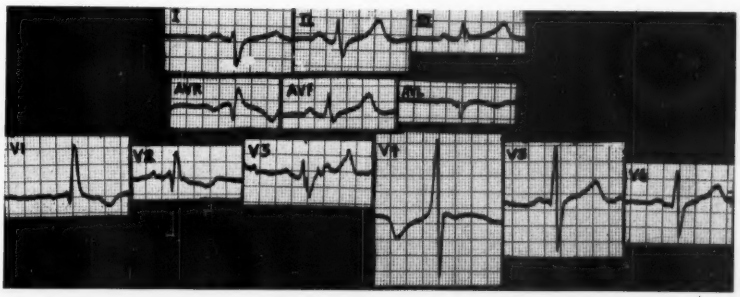

Fig. 13.—Case 5. Preoperative electrocardiograph showing an incomplete right bundle branch block with evidence of right ventricular hypertrophy. There is no evidence of left ventricular hypertrophy. (Paper speed, 50 mm./sec.)

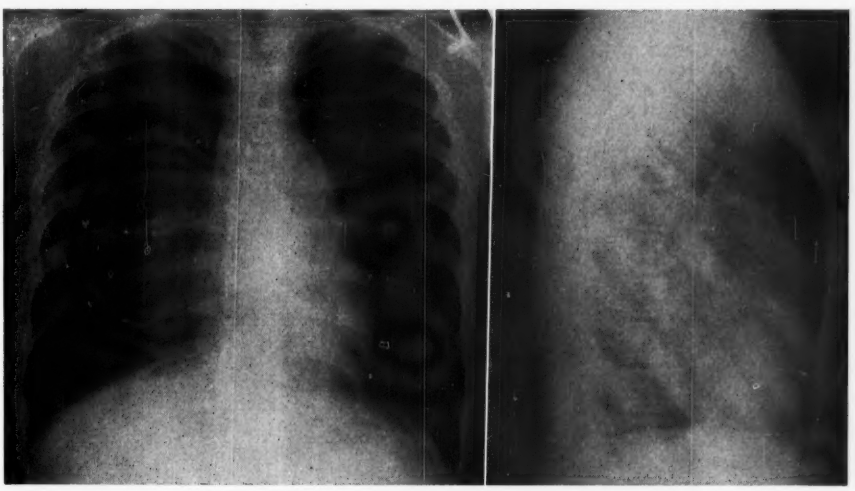

Fig. 14.—Case 5. PA and right lateral chest roentgenograms showing a normal transverse heart diameter with right ventricular enlargement. The pulmonary conus is prominent, the right pulmonary artery is enlarged, but the peripheral lung fields are clear. These are the typical findings in individuals with irreversible vascular changes and right-to-left shunting.

At the first-stage operation, an abbreviated incision was first made through the right fourth intercostal space and a generous lung biopsy was obtained from the upper lobe for frozen section examination. The vascular changes appeared to be only moderately severe (Fig. 15), and so the operation was continued. The right ventricle was markedly hypertrophied. The pulmonary artery was enormous and very tense, and it was feared that an attempt at partially excluding its lumen with a clamp might tear it. Therefore, the bypass was instituted and, with a partial exclusion clamp on the aorta and pulmonary artery, elliptical pieces of tissue were removed from each. An aortic homograft, 12 mm. in diameter, was easily and quickly anastomosed to each great vessel. The aorta was then cross-clamped distal to the graft site and, aided by potassium citrate arrest, a 17 mm. interventricular septal defect

was closed with a double-thickness Teflon cloth patch. The oozing from the graft suture lines was troublesome, but after the protamine had taken effect, and with the insertion of additional sutures, good hemostasis was finally obtained. Postoperatively, the child was alert and, during the first 24 hours, he seemed to be progressing satisfactorily. A soft systolic murmur could be heard over the upper end of the sternum. Approximately 28 hours postoperatively, his

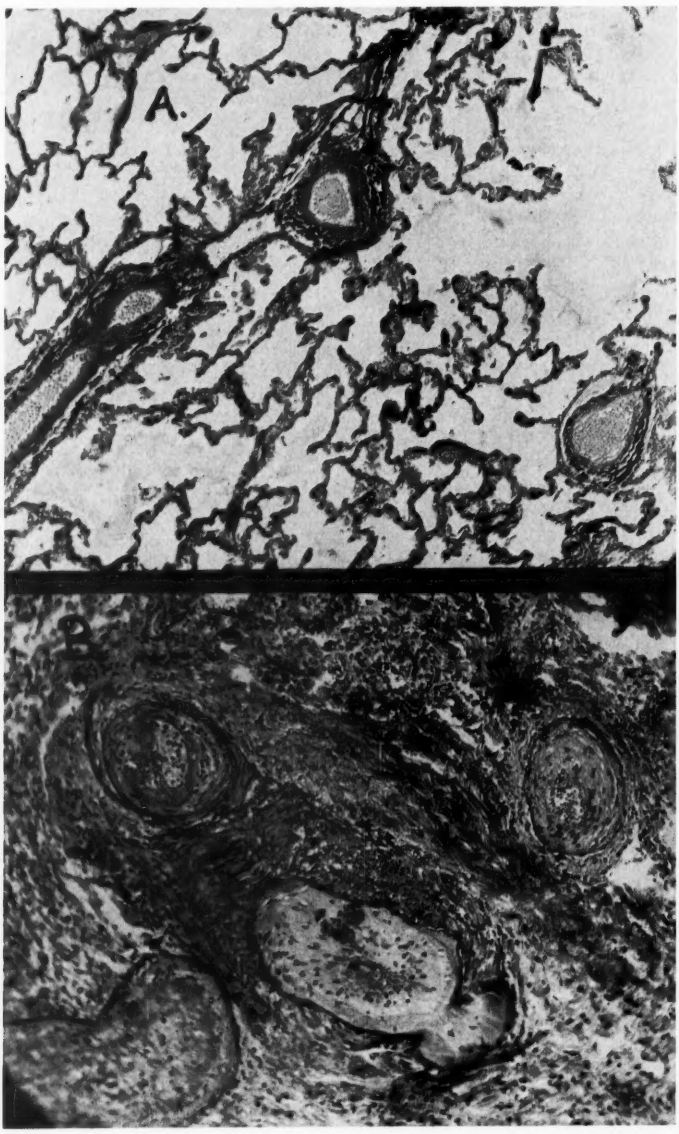

Fig. 15.—Case 5. *A*, Surgical biopsy showing dilated arteries with atrophic media compared with, *B*, tissue obtained at autopsy from a more central area of the lung. The irreversible vascular changes seen in the "Eisenmenger lung" are well demonstrated (× 100).

general condition began to deteriorate. His blood pressure dropped, and the pulse and respiration rose. The murmur could no longer be heard. His condition continued to deteriorate and he died 2 hours later.

Comment: This patient was undoubtedly of the Eisenmenger type with advanced, irreversible vascular changes and a minimal left-to-right shunt. Evidence for this was the x-ray appearance of a small heart, the practically normal fluoroscopic appearance of the activity of the pulmonary arteries, and a minimal step-up in saturation of the right ventricular blood sample. The suggestive early desaturation of the arterial blood and the high hemoglobin value were additional corroborative evidence. He should not have been selected for the operation. Furthermore, it is probable that this patient would not have tolerated later closure of the "ductus" even if he had survived the first stage.

At autopsy, clotting of the graft was confirmed. This is not surprising in view of the very small flow which passed across it.

It was interesting to see the discrepancy between the histopathologic appearance of the lung tissue obtained by lung biopsy (Fig. 15, *A*) and that obtained at autopsy from a more central portion of the lung (Fig. 15, *B*). As Edwards[7] has pointed out, dilated and atrophic vessels may be found distal to the advanced occlusive changes found in the Eisenmenger lung. Thus, if this is not kept in mind, especially when none of the severely afflicted arteries are seen, the biopsy may be misinterpreted.

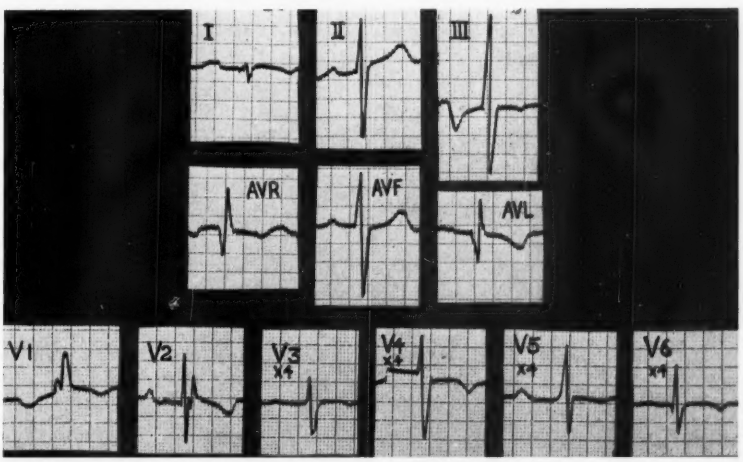

Fig. 16.—Case 6. Preoperative electrocardiogram indicates hypertrophy of both right and left ventricles. (Paper speed, 50 mm./sec.)

CASE 6.—B. McC., a 5-year-old girl, had been admitted to the Children's Hospital 2 years previously for the repair of a cleft palate and harelip. In addition to a heart murmur, a double kidney and hemivertebrae were found. The child suffered from repeated respiratory infections and had a decreased exercise tolerance.

She was below the third percentile in growth. There was a Grade 3 (1-4) systolic murmur present which was loudest in the fourth left intercostal space and was transmitted over the entire precordium. P_2 was accentuated.

The electrocardiograph (Fig. 16) showed both right and left ventricular hypertrophy. A teleoroentgenogram (Fig. 17) demonstrated the enlarged heart and an accentuation of the pulmonary vascularity. On fluoroscopy, the pulmonary artery activity was considered to be moderately increased—slightly more than the other similar cases in this series. Cardiac catheterization was performed (Table VI). The diagnosis was made of interventricular septal defect with equal-pressure pulmonary hypertension and significant left-to-right shunt. She was discharged to await readmission for the two-stage operation.

Fig. 17.—Case 6. PA and right lateral chest roentgenograms showing cardiac enlargement and marked accentuation of the pulmonary vascularity.

Fig. 18.—Case 6. Autopsy photograph of the posterior aspect of the heart with the pulmonary artery (*left*) and aorta (*right*) opened. The narrow orifices produced by the longitudinal incisions are well illustrated. Both anastomotic sites are clotted.

On Feb. 7, 1958, the first stage was undertaken. Because of the technical difficulties at the second stage in Case 4, a nylon graft (Edwards-Tapp), ⅜ inch inside diameter, was placed between the ascending aorta and pulmonary artery. Each time an ample segment of aorta was excluded by the clamp, a fall in blood pressure occurred. Therefore, instead of removing an elliptical piece of tissue, it was decided to resort to a longitudinal incision in the aorta. Although mindful of the previous experience in Case 2, it was thought that the

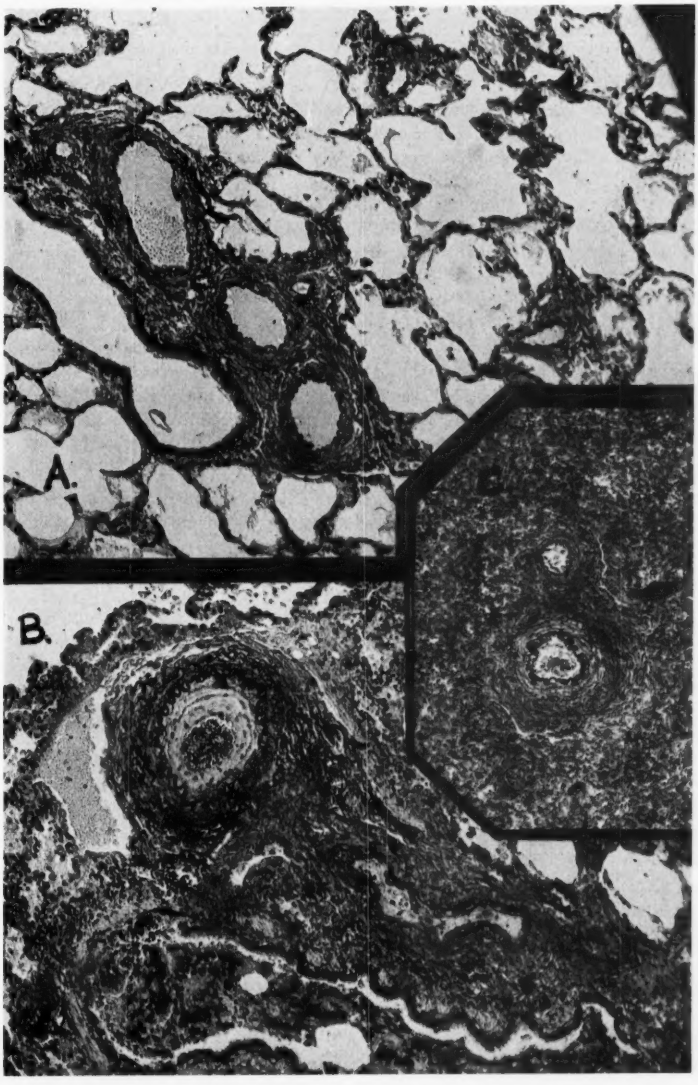

Fig. 19.—Case 6. *A*, Photomicrograph of peripheral biopsy obtained at surgery. *B* and *C*, Photomicrographs of more centrally located tissue obtained after the patient's death. The changes appear more severe than in *A*.

TABLE VI

B. MC C.	PREOPERATIVE	
	SATURATION PER CENT	PRESSURE (MM. HG)
Superior vena cava	69	
Right atrium	68	6.5
Right ventricle	85	84/0
Main pulmonary artery	89	84/36
Brachial artery	100	84/52

Case 6. Preoperative studies indicating a large shunt at the ventricular level and equal-pressure pulmonary hypertension.

large diameter of the graft would compensate for failure to remove elliptical pieces of vessel wall and assure patency at least for a sufficient time to permit recovery. The bypass was established and, employing potassium citrate arrest, a 17 mm. septal defect was closed with a Teflon cloth patch. Following perfusion, the patient's condition appeared satisfactory. She was alert, her color was good and the vital signs were stable. A loud systolic shunt murmur could be heard over the upper end of the sternum. The blood pressure was 105/55 mm. Hg, typically a wide pulse-pressure ductus type. Suddenly, 3½ hours after surgery, in a matter of seconds, her condition dramatically changed. Her skin became pale, the blood pressure became unobtainable, and the pulse and respiration rose. Coincidentally, it was noted that the shunt murmur had disappeared. It was suspected that the graft had become clotted and that this had precipitated the sudden reversal in the patient's condition. With the aid of resuscitative measures, including small amounts of blood and vasopressors, the child rallied and the blood pressure returned to 80/60 mm. Hg. However, the child continued to appear "shocky." Her color remained poor and the fast pulse and respiration persisted. The shunt murmur never returned. The child continued in this fashion for another 7½ hours and then died.

Comment: This child had the largest left-to-right shunt in the entire series as demonstrated by fluoroscopic study and the step-up in saturation of the right ventricular sample. This evidence of high flow might have led one to predict preoperatively that the child could have survived a single-stage approach. However, bedside observations made during the postoperative period established that the functioning "ductus" was necessary and that its occlusion by thrombus (Fig. 18) precipitated the sudden and fatal cardiovascular deterioration. One might take the opposite view that shock occurred suddenly causing the murmur to disappear and the other events which followed. Unfortunately, under these circumstances it is not practical to obtain suitable objective data. One must rely instead upon clinical impressions. In support of the first explanation was the suddenness with which the patient's condition changed after a satisfactory earlier postoperative response. This behavior contrasts sharply with those similar cases treated by one-stage surgery who show evidence of a failing circulation as soon as the bypass is discontinued. These early signs are readily recognized and soon produce a clinical picture similar to the one presented by this child after the graft became clotted. In our experience, their appearance presages an imminent fatal outcome.

The histologic sections showed moderately severe vascular changes. Those obtained at autopsy from the central areas (Fig. 19, *B* and *C*) of the lung appear more pronounced than those found in the tissue obtained by surgical biopsy (Fig. 19, *A*).

DISCUSSION

The initial event occurring after conventional corrective surgery that is responsible for the ultimate death of these equal-pressure pulmonary hypertensive patients has not been precisely identified. There may arise an exaggerated vasospastic component which superimposes itself on the already abnormal

arterial bed. The medial hypertrophy seen on microscopic examination would suggest that the muscular arteries are indeed capable of a vigorous vasomotor reaction. Perhaps this response is precipitated by suddenly removing the excessive pulmonary blood flow or by the manipulation of the lungs. When this is added to those other burdens imposed by suddenly reversing the adapted state and by extensive surgery on the heart itself, the cardiopulmonary system may very likely be overwhelmed. Therefore, if these patients are to survive operation it would seem reasonable (1) to avoid an immediate alteration of this compensated state by achieving the desired result gradually in two stages, and (2) to plan the two stages so that the least physiologic readjustment will be required at the time of the greatest operative undertaking. This can be accomplished if, at the first stage, an ample left-to-right flow is perpetuated by using a graft of large diameter and by being careful with details of the anastomoses to assure patency. Anastomoses made to longitudinal incisions, a technique which has been used successfully in the past in other vascular procedures, have produced clotting of the "ductus" in these patients. This difference in results is probably due to the special conditions of blood flow across the graft. Even though it may have the same diameter as the septal defect, the left-to-right shunt will still be reduced by the influence of other factors governing flow in tubes, such as length and contour of the graft, the characteristics of its internal surface and the configuration of the anastomotic orifices.

The second stage is performed 3 to 6 months later, after the heart and lungs have recovered from the initial operative intervention. Thus, the more physiologically strenuous burden imposed on the cardiopulmonary system by completely abolishing the shunt will be made to coincide with an operative procedure equal to closing a patent ductus.

Because of the various combinations of plumonary flow and resistance which may interact to cause elevation of the pulmonary artery pressures to systemic levels, those patients with equal-pressure pulmonary hypertension constitute a physiologically heterogeneous group. This has been well documented by Dammann[8] and Edwards.[7] Therefore, although the term "equal-pressure" may be used for roughly categorizing a special group of individuals with pulmonary hypertension, it is an inadequate index for selecting patients for the two-stage operation. Those patients who are acceptable must still have a significant left-to-right shunt (Fig. 20). This selection is guided by the degree of increase over normal in the activity exhibited by the pulmonary arteries during fluoroscopy. The greater the role being played by the factor of flow through the lungs, the more expansile the pulmonary arteries and their branches become (in the absence of pulmonic insufficiency). However, it should be noted that this accentuation is not of the magnitude seen in patients with lesser degrees of pressure elevation. Also of help is the amount of increase (over that from the right atrium) in the saturation of the right ventricular blood sample obtained during catheterization. A value around 10 per cent is a favorable sign.

The remaining members of the equal-pressure group who have minimal left-to-right shunt-flow or persistent flow-reversal are not suitable candidates for

the two-stage operation (Fig. 21). This transition from a significant left-to-right shunt seems to occur as the child approaches puberty. So far, none of the equal-pressure cases in this age range (or older) have been found acceptable. Histologic study of lung sections obtained from some of these patients has strengthened the impression that age is another important criterion for the proper selection of cases for the two-stage operation.

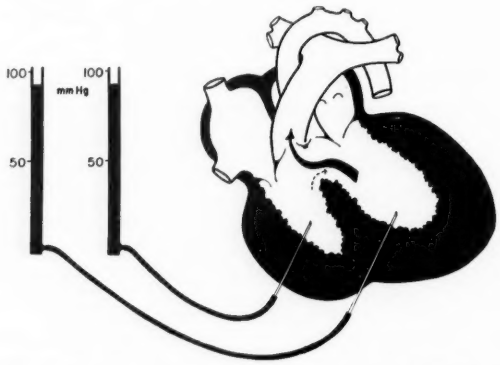

Fig. 20.—Schematic representation of the pathophysiology in an "equal-pressure" pulmonary hypertensive with residual left-to-right shunt. Here flow is still a factor in the pressure elevation. This type of patient is acceptable for the two-stage procedure.

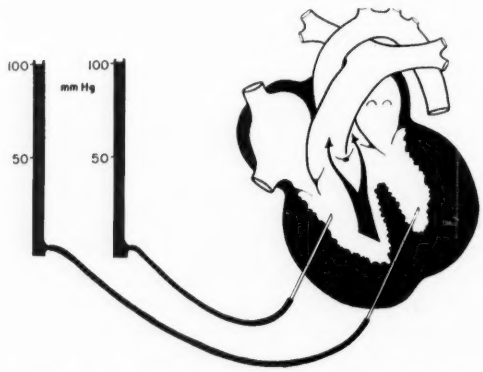

Fig. 21.—A representation of an "equal-pressure" patient in whom pulmonary resistance has exceeded systemic resistance. There is now a right-to-left shunting of blood (Eisenmenger's syndrome). This patient is not acceptable for the two-stage procedure.

SUMMARY

A two-stage operation is proposed for the surgical correction of ventricular septal defects associated with equal-pressure pulmonary hypertension. At the first stage, a large diameter graft, serving as a temporary artificial "ductus," is placed between the ascending aorta and the pulmonary artery and, with the aid of a mechanical heart-lung apparatus, the septal defect is repaired. The second stage is performed 3 to 6 months later and consists of dividing the graft, thus

completing the correction of the shunt. This approach is predicated on the principle of separating the burdens on the heart and lungs imposed by an operation of open-heart magnitude from those imposed by suddenly reversing the patient's compensated pathophysiologic state. At Stage I, the cardiovascular system is called upon to make a minor physiologic readjustment coincident with an operation of great magnitude. Conversely, at Stage II, the burden is similarly minimized by using a lesser surgical procedure when the demands of physiologic compensation are likely to be most severe.

The proper selection of cases depends upon choosing those patients with equal-pressure with a significant left-to-right shunt. The most helpful guides have been the activity of the pulmonary artery, as determined fluoroscopically, and the catheterization data. Age is also an important factor. The results so far have been encouraging in that 3 of the 5 properly selected patients have survived. Follow-up catheterization studies have shown a return to normal hemodynamics.

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EDITOR'S NOTE: The discussion of the preceding paper (Sirak and Hosier) will be published in an upcoming issue following the paper entitled "Corrective Surgery in the Presence of Far Advanced Pulmonary Hypertension," by Dr. C. Walton Lillehei and associates, with which it was discussed.

SURGICAL TREATMENT FOR THE TETRALOGY OF FALLOT BY OPEN INTRACARDIAC REPAIR

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THE PROGRESSING invalidism usually imposed by the combination of malformations known as the "tetralogy of Fallot" has long stimulated search for effective treatment. Wide acclaim properly greeted the discovery of Blalock and Taussig[1] that an anastomosis between a systemic and pulmonary artery resulted in amelioration of cyanosis and polycythemia and improved exercise tolerance in the patient with tetralogy of Fallot. The beneficial effect of increased pulmonary blood flow was again demonstrated in the results obtained by Potts[2] utilizing anastomosis of the aorta and pulmonary artery. Brock[3] logically argued that pulmonary flow could be increased by directing the surgical endeavor toward relief of the pulmonary stenosis. He showed that good palliation could be achieved in many patients by pulmonary valvotomy and infundibular resection done by a closed technique. Many surgeons dreamed of complete repair of the tetralogy of Fallot, but it was first accomplished by Lillehei and associates in 1954 using whole body perfusion established by the technique of controlled cross-circulation.[4]

General agreement has not been reached as yet concerning the surgical technique of choice for the treatment of the tetralogy of Fallot. Experience with patients treated by open intracardiac repair at the Mayo Clinic since April, 1955, has led us to conclude that this is an effective treatment for tetralogy of Fallot. Data concerning these cases and a discussion of them form the basis for this report.

DEFINITION

Since there is a wide variation among hearts with pulmonary stenosis and ventricular septal defect, it appears unreasonable to designate them all as the tetralogy of Fallot. Apparent dextroposition of the aorta occurs in some patients with ventricular septal defect and no pulmonary stenosis and there may be no dextroposition in a few patients seeming to have otherwise typical tetralogy of Fallot. This feature does not then serve well to identify the tetralogy of Fallot. It has been suggested that the term "tetralogy of Fallot" be discarded

From the Mayo Clinic and Mayo Foundation.

Read at the Thirty-eighth Annual Meeting of The American Association for Thoracic Surgery, Boston, Mass., May 16-18, 1958.

in recognition of the fact that this condition shades off toward severe pulmonary stenosis with a very small ventricular septal defect or toward a large ventricular septal defect with mild pulmonary stenosis.

Clinically and surgically, the term continues to have sufficient usefulness to justify its retention. For this study, tetralogy of Fallot is defined as a congenital cardiac malformation with ventricular septal defect of a size approximating the aortic orifice and pulmonary stenosis of such severity that it, in combination with the ventricular septal defect, results in identical right and left ventricular pressures. There are varying degrees of dextroposition, or overriding of the aorta, in specimens meeting these criteria. The pulmonary stenosis is usually infundibular, either isolated or in combination with stenosis of the pulmonary valve.[5, 6] Rarely, the stenosis is limited to the pulmonary valve.

In most patients with tetralogy of Fallot, high resistance to right ventricular emptying is posed by the pulmonary stenosis, the direction of the shunt across the ventricular septal defect is right to left and, as a result, cyanosis is present. When the resistance posed by the pulmonary stenosis is less severe, the shunt may be bidirectional. Uncommonly, the resistance posed by the stenosis is sufficiently low that only a left-to-right shunt occurs, although pressures in the two ventricles are identical. Since some patients who were acyanotic early in life are cyanosed in later childhood, it is assumed that the relative severity of the pulmonary stenosis can increase.

MATERIAL AND METHODS

All patients except one with the tetralogy of Fallot undergoing operation on one surgical service at the Mayo Clinic since April 1, 1955, were treated by open intracardiac repair. For the one exception, a severely handicapped woman 28 years old, operated on in the summer of 1955, the Brock infundibular resection was done. All the patients treated on this service by open intracardiac repair until May 1, 1958, are included in this report.

Data concerning all patients treated by open intracardiac repair on this service in this period are given in Table I. Remarks concerning disability and cyanosis are based on the history and physical examination. Associated defects and previous operations are noted there. The anatomy of the pulmonary stenosis given in the table was determined at operation. When the pulmonary artery was so narrow that it seemed to offer significant resistance to right ventricular emptying, it is listed as an obstructing lesion.

Data concerning patients surviving operation and hospitalization are shown in Table II. The present status and cyanosis given in this table are those determined by history and examination. A clinical evaluation was made of the repair of the ventricular septal defect on the basis of the auscultation and roentgenography of the thorax at postoperative examinations. The possible limitations of this type of evaluation are recognized. It is doubtful, however, that large residual shunts can be present without clinical manifestations. Postoperative catheterization data when available were used. Evaluation of the

TABLE I. OPEN INTRACARDIAC REPAIR FOR

CASE†	AGE, YEAR	SEVERITY OF DISABILITY	CYANOSIS		ARTERIAL O_2 SATURATION (PER CENT)		ADDITIONAL DEFECTS OR PREVIOUS OPERATION	SITE OF PULMONARY STENOSIS		
			REST	EXERCISE	REST	EXERCISE‡		INFUNDIBULUM	VALVE§	PA
1	5	Sev.	Mod.	Sev.			Left subclavian A. to PA anastomosis (1951)	+	–	–
2	4	Sev.	Sev.	Sev.	70	44		+	+	–
3	7	Sev.	Mild	Mod.				+	–	–
4	17	Mod.	None	Mod.				+	+	–
5	3	Sev.	Mild	Mod.	92	86		+	+	+
6	8	Mod.	Mild	Mod.	89	83		+	+	–
7	11	Sev.	None	Mild				+	+	–
8	5	Mod.	Mild	Sev.	84	61	Agenesis of Left PA	–	+	–
9	6	Sev.	Mod.	Sev.	86	67		+	+	–
10	7	Sev.	Sev.	Sev.				+	+	+
11	28	Mod.	None	None	95			+	–	–
12	2	Mod.	Mod.	Sev.	78	61		+	+	–
13	5	Sev.	Mod.	Sev.	81	56		+	–	–
14	13	Sev.	Mod.	Sev.	80	49	Left subclavian A. to PA anastomosis (1948)	+	–	–
15	3	Mod.	Mod.	Sev.	82	75		+	+	–
16	17	Mod.	None	Mod.	97	69		+	+	–

TETRALOGY OF FALLOT: ALL 74 CASES*

METHOD OF REPAIR				PRESSURES MEASURED IN OPERATING ROOM AFTER REPAIR, MM. Hg				
	PULMONARY STENOSIS							
VSD§	RESECTION AND/OR VALVOTOMY	OUTFLOW TRACT (IVALON)	COMPLETE IVALON RECONSTRUCTION‖	PA	RV	AORTA	HOSPITAL FATE	PROBABLE CAUSE OF DEATH
	+	–	–				Died 2 hr. p.o. with pulm. edema	Perfusion; VSD repair complete at necropsy
Ivalon (early method)	+	–	–				Died 10 hr. p.o. with pulm. edema	Related to perfusion and incomplete repair of VSD
Ivalon (early method)	+	–	–				Died at end of operation	Heart block
	+	–	–				Died 8 hr. p.o.	Hemorrhage, related to perfusion
Ivalon (early method)	+	–	–				Died 4 hr. p.o.	Perfusion; incomplete relief of pulmonary stenosis
Ivalon (early method)	+	–	–				Survived	
Ivalon (early method)	+	–	–				Survived	
Ivalon (early method)	+	–	–				Survived	
Ivalon (early method)	+	–	–	34/15	100 / 10-18	86/53 (radial)	Survived	
Ivalon (early method)	+	–	–		124/18	38/29	Died at end of operation	Incomplete relief of pulmonary stenosis
Ivalon (early method)	+	–	–	23/8	45/0	64/35	Survived	
Ivalon (early method)	+	–	–				Died 12 hr. p.o.	Heart block; incomplete repair of VSD, probably incomplete relief of pulmonary stenosis
Ivalon (early method)	+	–	–				Survived	
Ivalon (early method)	+	–	–	32/7	52/5	77/85	Died 12 hr. p.o.	Incomplete repair VSD
Direct suture	+	+	–	24/12	53/7	81/58	Survived	
Ivalon (early method)	+	+	–	19/8	22/4	70/30	Survived	

TABLE I

CASE†	AGE, YEAR	SEVERITY OF DISABILITY	CYANOSIS		ARTERIAL O_2 SATURATION (PER CENT)		ADDITIONAL DEFECTS OR PREVIOUS OPERATION	SITE OF PULMONARY STENOSIS		
			REST	EXERCISE	REST	EXERCISE‡		INFUNDIBULUM	VALVE§	PA
17	7	Mod.	None	Mild	95	87		+	–	–
18	9	Sev.	Mild	Sev.	87	65	Atrial septal defect	+	+	+
19	11	Mod.	None	None				+	–	–
20	9	Mild	None	None	97			+	–	–
21	14	Sev.	Mild	Sev.	92	61		+	–	–
22	15	Sev.	Mild	Mod.	90	79		+	–	–
23	6	Mild	None	None				+	+	–
24	3	Sev.	Mod.	Sev.	79	49		+	–	+
25	6	Sev.	Mod.	Sev.	80	44	Patent ductus arteriosus from which originated left subclavian A.	+	–	–
26	4	Sev.	None	Mod.				+	+	–
27	19	Mod.	None	Slight	95	93		+	+	–
28	7	Sev.	Mod.	Sev.	72	58		+	–	–
29	8	Mod.	Mild	Mod.	90	51		+	+	–
30	6	Sev.	Mild	Mod.	93	85	Left subclavian to PA anastomosis (1953)	+	+	+
31	9	Sev.	Mild	Mod.	82		Persistent left superior vena cava	+	+	–
32	1⅝	Sev.	Mod.	Sev.	66	50	Agenesis left coronary A. with anomalous right coronary A.	+	+	+
33	24	Sev.	None	None	95			+	+	–

TABLE I (CONT'D)

METHOD OF REPAIR				PRESSURES MEASURED IN OPERATING ROOM AFTER REPAIR, MM. Hg			HOSPITAL FATE	PROBABLE CAUSE OF DEATH
	PULMONARY STENOSIS							
VSD§	RESECTION AND/OR VALVOTOMY	OUTFLOW TRACT (IVALON)	COMPLETE IVALON RECONSTRUCTION‖	PA	RV	AORTA		
Ivalon (early method)	+	–	–	18/2	23/1	105/56	Survived	
Ivalon (early method)	+	+	+	24/6	45/0	70/35	Survived	
Ivalon (early method)	+	–	–	37/15	42/10	95/32	Survived; temporary heart block	
Ivalon (early method)	+	–	–	20/7	24/0	95/50	Died 12 hr. p.o. of progressive hypertension	Cardiac tamponade
Ivalon	+	–	–				Survived	
Ivalon	+	–	–	36/9	44/0	106/60	Survived	
Ivalon	+	–	–	17/10	20/0	75/44	Survived	
Ivalon	+	+	–	32/15	57/0	85/57	Died 14 hr. p.o.	In part, perfusion (probable hypovolemia); in part, incomplete relief of pulmonary stenosis
Ivalon	+	+	–	38/17	43/8	85/52	Died 3 hr. p.o.	Artifically created systemic hypertension
Direct suture	+	–	–		35/4	98/42	Survived	
Ivalon	+	–	–	15/2	40/5	78/46	Survived; temporary heart block	
Direct suture	+	–	–	35/12	51/11	62/27	Died 7 hr. p.o.	Poor perfusion, surgery therefore done in haste and poorly; heart block; incomplete relief of pulmonary stenosis
Ivalon	+	–	–	25/10	42/0	65/37	Survived	
Ivalon	+	+	–	27/5	35/2	75/40	Survived	
Direct suture	+	–	–	27/7	30/0	85/50	Survived	
Ivalon	+	+	+	16/4	35/0	57/20	Died at end of operation	Division of single coronary artery
Ivalon	+	–	–	16/10	32/4	95/60	Survived	

TABLE I

CASE†	AGE, YEAR	SEVERITY OF DISABILITY	CYANOSIS		ARTERIAL O_2 SATURATION (PER CENT)		ADDITIONAL DEFECTS OR PREVIOUS OPERATION	SITE OF PULMONARY STENOSIS		
			REST	EXERCISE	REST	EXERCISE‡		INFUNDIBULUM	VALVE§	PA
34	9	Mod.	Mod.	Mod.	82	81		+	+	+
35	31	Sev.	Mod.	Sev.	65	40		+	+	–
36	5	Mod.	Mild	Mod.			Diabetes mellitus	+	+	–
37	1¼	Sev.	Mild	Sev.	86	69		+	+	–
38	5	Mod.	None	Mod.	91	79	Persistent left superior vena cava	+	+	–
39	35	Mod.	None	Mild	96		Small persistent left superior vena cava	+	+	–
40	5	Mild	None	None	97			+	–	–
41	8	Sev.	None	Sev.	95	64		+	+	+
42	6	Sev.	Sev.	Sev.	78	57	Potts' anastomosis (1953) and previous Brock operation (1954)	+	–	–
43	3	Sev.	Mod.	Sev.				+	+	+
44	13	Sev.	Mild	Mod.	91	73	ASD; anomalous right coronary A.	+	–	–
45	17	Sev.	Sev.	Sev.			None	+	+	–
46	8/12	Sev.	Mod.	Mod.	87	78		+	+	–
47	21	Sev.	Mod.	Sev.				+	+	–
48	7	Mod.	None	Mod.	95	80		+	–	–
49	7	Sev.	Mild	Mod.	95	61	Large azygos and hemiazygos veins; small IVC	+	+	–
50	20	Sev.	Mod.	Sev.	81	61		+	–	–
51	10	Mod.	Mild	Mod.	94	85	Small patent ductus arteriosus	+	+	–
52	11	Mod.	Mod.	Sev.	80		Anomalous right coronary A. supplying left ant. desc. coronary A. (preserved)	+	–	–
53	2½	Sev.	Mod.	Mod.	84	73		+	+	+
54	7	Sev.	Sev.	Sev.	68	43		+	+	–

TABLE I (CONT'D)

METHOD OF REPAIR				PRESSURES MEASURED IN OPERATING ROOM AFTER REPAIR, MM. Hg				
	PULMONARY STENOSIS							
VSD§	RESECTION AND/OR VALVOTOMY	OUTFLOW TRACT (IVALON)	COMPLETE IVALON RECONSTRUCTION‖	PA	RV	AORTA	HOSPITAL FATE	PROBABLE CAUSE OF DEATH
Direct suture	+	–	–		80/5	80/50	Survived	
Ivalon	+	+	–	35/15	37/2	85/44	Died 24 days p.o.	Pseudomonas endocarditis and bacteremia
Direct suture	+	–	–	40/27	80/27	68/25	Died 12 hr. p.o.	Inadequate relief of pulmonary stenosis
Direct suture	+	–	–				Survived	
Direct suture	+	+	–		55/10	100/55	Survived	
Ivalon	+	–	–	25/16	40/11	81/51	Survived	
Direct suture	+	–	–	21/6	25/4	75/44	Survived	
Ivalon	+	+	+	24/14	61/9	108/62	Survived	
Ivalon	+	+	–		34/4	92/47	Survived	
Ivalon	+	+	+	20/10	37/6	75/42	Survived	
Ivalon	+	–	–	18/7	36/6	115/91	Died 48 hr. p.o.	Division of anomalous right coronary A. supplying left anterior desc. coronary A.
Ivalon	+	+	+	34/8	47/5	90/48	Survived	
Direct suture	+	+	–		52/10	71/40	Died 3 hr. p.o.	Perfusion
Ivalon	+	+	–	27/17	48/9	65/40	Survived	
Direct suture	+	–	–	23/10	27/4	79/44	Survived	
Direct suture	+	+	+	23/11	53/3	100/60	Survived	
Direct suture	+	–	–	29/14	38/26	99/61	Survived	
Direct suture	+	–	–	25/11	37/7	104/54	Survived	
Ivalon	+	–	–	34/9	38/4	108/62	Survived	
Direct suture	+	+	+				Survived	
Direct suture	+	–	–	32/12	65/11	80/55	Died 36 hr. p.o.	Incomplete relief of pulmonary stenosis

TABLE I.

CASE†	AGE, YEAR	SEVERITY OF DISABILITY	CYANOSIS		ARTERIAL O_2 SATURATION (PER CENT)		ADDITIONAL DEFECTS OR PREVIOUS OPERATION	SITE OF PULMONARY STENOSIS		
			REST	EXERCISE	REST	EXERCISE‡		INFUNDIBULUM	VALVE§	PA
55	12	Mild	None	None	97	95		+	−	−
56	4	Sev.	Sev.	Sev.	65		Anomalous right coronary A. supplying left ant. desc. coronary A. (preserved)	+	+	+
57	27	Mod.	Mod.	Mod.				+	+	−
58	9	Sev.	Mod.	Sev.	83	60		+	+	+
59	3	Sev.	Mod.	Sev.	83	78		+	+	+
60	5	Sev.	Mod.	Sev.	74	37		+	−	−
61	16	Sev.	Mild	Mod.				+	−	−
62	1⅝	Sev.	Mild	Sev.	85	53		+	+	+
63	23	Mod.	Mild	Mod.	92	86		+	+	+
64	3	Sev.	Mild	Mod.	89	81	ASD	+	+	−
65	5	Mod.	Mod.	Mod.	84	73		+	+	−
66	3	Mod.	Mod.	Sev.	78	68		+	+	+
67	6	Mod.	Mild	Mod.	89	81	ASD	+	+	−
68	4	Mod.	Mild	Mod.	92	85	ASD	+	+	−
69	5	Sev.	Mod.	Mod.	87	76	Small patent ductus arteriosus	+	+	+
70	5	Mod.	Mild	Mild				+	+	−
71	17	Mod.	Mild	Mod.	89		Situs inversus	+	+	−
72	6	Mod.	Mod.	Sev.	70	58		+	−	−
73	10	Sev.	Mod.	Mod.	85	71	Associated ASD; left subclavian to PA anastomosis (1950); brain abscess (1956)	+	+	−
74	29	Mod.	Mild	Mod.			Left subclavian to PA anastomosis (1956)	+	+	−

*Abbreviations used in this table and in Table II are: PA = pulmonary artery; VSD = ventricular septal defect; RV = right ventricle; A. = artery; AV = atrioventricular; IVC = inferior vena cava; ASD = atrial septal defect; Sev. = severe; Mod. = moderate.

†In a previous article,[7] deaths due to perfusion were analyzed. Cases in which death occurred considered in that article and also in this one are Cases 1, 2, 3, 4, 5, 9, 12, 14, 20, 24, 25, 28, 32, 35, 36, 44, and 46. In the previous article the cases were listed as Cases 6, 9, 10, 15, 16, 47, 63, 86, 103, 117, 125, 134, 158, 161, 165, 202 and 205, respectively.

(CONT'D)

METHOD OF REPAIR				PRESSURES MEASURED IN OPERATING ROOM AFTER REPAIR, MM. Hg				
	PULMONARY STENOSIS							
VSD§	RESECTION AND/OR VALVOTOMY	OUTFLOW TRACT (IVALON)	COMPLETE IVALON RECONSTRUCTION‖	PA	RV	AORTA	HOSPITAL FATE	PROBABLE CAUSE OF DEATH
Direct suture	+	–	–	32/15	35/7	105/60	Survived	
Ivalon	+	–	–	34/15	54/7	86/41	Died 7 hr. p.o.	Probable myocardial failure (present preoperatively) possibly long (45 min.) asystole; necropsy showed complete repair
Ivalon	+	–	–	25/10	36/10	98/58	Survived	
Ivalon	+	+	+	28/14	48/10	91/57	Died 5 hr. p.o.	Uncertain. Myocardial failure (?); asystole 46 min. (?)
Direct suture	+	+	+	28/5	41/6	112/68	Survived	
Ivalon	+	+	–	30/10	34/0-4	82/47	Survived	
Direct suture	+	–	–	19/12	25/6	74/48	Survived	
Direct suture	+	+	+	26/10	42/5	90/55	Survived	
	+	+	+				Survived	
Direct suture	+	+	+	28/11	36/9	86/34	Died 13 days p.o.	Probably chronic heart failure to which AV dissociation contributed
Ivalon	+	+	–	27/12	49/9	105/73	Survived	
Ivalon	+	+	+	23/10	56/7	86/55	Survived	
Ivalon	+	+	–	13/7	28/8	73/4	Survived	
Ivalon	+	+	–	20/10	32/8	99/53	Survived	
Ivalon	+	+	–	44/9	73/5	86/39	Survived; permanent but asymptomatic heart block	
Direct suture	+	+	–	28/6	45/5	85/47	Survived	
Ivalon	+	+	–	22/5	34/5	75/48	Survived	
Direct suture	+	–	–	21/8	44/5		Survived	
Direct suture	+	+	–	25/11	36/10	95/47	Survived; temporary heart block	
Direct suture	+	–	–	18/7	56/4		Survived	

‡Mild exercise on a treadmill for 5 min. at about 1½ miles per hour.

§Induced cardiac asystole employed first in Case 21 and routinely thereafter.

‖Complete Ivalon reconstruction indicates that the cardiotomy incision was carried across the pulmonary valve ring and onto the pulmonary artery and a prosthesis was placed in this area as well as in outflow tract of right ventricle.

TABLE II. FOLLOW-UP DATA ON PATIENTS

CASE	MONTHS BETWEEN OPERATION AND LAST EXAMINATION	STATUS AT LAST EXAMINATION					CLINICAL EVALUATION OF REPAIR	
			CYANOSIS		ARTERIAL O_2 SATURATION (%)			
		SYMPTOMS	REST	EXERCISE	REST	EXERCISE*	VSD	PULMONARY STENOSIS
6	29	Asymptomatic; full activity	None	None			Probable moderate L-to-R shunt	Fair
7	24	Asymptomatic; full activity	None	None			Complete	Good
8	16	Asymptomatic; full activity	None	None	95	95	Complete	Good
9	24	Asymptomatic; full activity	None	None	99		Complete	Good
11	7	Asymptomatic; full activity	None	None			Complete	Good
13	18	Asymptomatic; full activity	None	None	98	95	Complete	Good
15	10	Asymptomatic; full activity	None	None			Possible small L-to-R shunt	Fair
16	22	Asymptomatic; full activity	None	None	97	94	Probable small L-to-R shunt	Complete
17	11	Asymptomatic; full activity	None	None	98†	94†	Complete	Good
18	21	Asymptomatic; full activity	None	None	97	95	Complete	Good
19	14	Asymptomatic; full activity	None	None			Probable small L-to-R shunt	Complete
21	2	Died at home	P.O. dye-dilution curve indicated incomplete repair of VSD with moderate L-to-R shunt; progressive cardiac enlargement occurred, with ultimate death; cause of death presumed to be cardiac failure from incomplete repair of VSD					
22	11	Asymptomatic; full activity	None	None	95	93	Complete	Complete
23	10	Asymptomatic; full activity	None	None			Complete	Complete
26	18	Asymptomatic; full activity	None	None	95	94	Complete	Complete
27	10	Occasional dizzy spells; otherwise asymptomatic	None	None			Complete	Good
29	14	Asymptomatic; full activity	None	None			Complete	Complete
30	9	Asymptomatic; full activity	None	None	96	97	Complete	Good
31	15	Asymptomatic; full activity	None	None			Complete	Complete
33		Died of Pseudomonas bacterial endocarditis						
34	2	Died of chronic intractable right heart failure which seemed to result from inadequate relief of pulmonary stenosis						

37	10	Asymptomatic; full activity	None	None			Complete	Good
38	8	Had been asymptomatic and in full activity when he died after a 6-hour illness characterized by cough and respiratory distress; no necropsy						
39	18	Asymptomatic; full activity	None	None			Small L-to-R shunt	Good
40	11	Asymptomatic; full activity	None	None			Complete	Complete
41	8	Asymptomatic; full activity	None	None	96	97	Complete	Good
42	5	Asymptomatic; full activity	None	None	95	97	Complete	Complete
43	10	Asymptomatic; full activity	None	None			Complete	Good
45	10	Asymptomatic; full activity	None	None	96†	93†	Complete	Good
47	10	Asymptomatic; full activity	None	None	98	95	Complete	Good
48	10	Asymptomatic; full activity	None	None	93†	92†	Complete	Complete
49	5	Asymptomatic; full activity	None	None	99†	97†	Complete	Fair
50	7	Asymptomatic; full activity	None	None	98	96	Complete	Complete
51	7	Asymptomatic; full activity	None	None			Complete	Good
52	6	Asymptomatic; full activity	None	None	96†	91†	Complete	Complete
53	6	Asymptomatic; full activity	None	None	92†	92†	Complete	Fair
55	3	Asymptomatic; full activity	None	None			Complete	Complete
57	5	Asymptomatic; full activity	None	None	96†	94†	Complete	Complete
59	3	Asymptomatic; full activity	None	None	96†	98†	Complete	Good
60	3	Asymptomatic; full activity	None	None	98†	98†	Complete	Complete
61	3	Asymptomatic; full activity	None	None	97†	93†	Complete	Complete
62	3	Asymptomatic; full activity	None	None	96†	97†	Complete	Complete
63		‡	None	‡			Complete	Good
65		‡	None	‡	97†	95†	Complete	Good
66		‡	None	‡	95	96	Complete	Fair
67		‡	None	‡			Complete	Good
68		‡	None	‡			Complete	Good
69		‡	None	‡			Incomplete	Poor
70		‡	None	‡	96†	96†	Complete	Good
71		‡	None	‡	96†	91†	Complete	Good
72		‡	None	‡			Complete	Good
73		‡	None	‡			Complete	Good
74		‡	None	‡			Complete	Good

*Mild exercise on a treadmill for 5 minutes at 1½ miles per hour.
†Indicates arterial oxygen studies were done 2 weeks after surgery.
‡Too recent to evaluate.

effectiveness of the operation for the pulmonary stenosis was made from review of the surgical records and pressures taken at operation and from data obtained at postoperative cardiac catheterization (Table III) when this was done. The arterial oxygen saturation studies given in Table II are those made at the end of the follow-up period unless otherwise indicated. Eleven patients (Cases 63 through 74) were operated on too recently to permit evaluation of the symptomatic status and cyanosis on exercise.

TABLE III. POSTOPERATIVE CARDIAC CATHETERIZATION STUDIES IN 7 CASES

CASE	INTERVAL SINCE OPERATION (MO.)	PRESSURE, MM. Hg				SHUNT
		POSTOPERATIVE CARDIAC CATHETERIZATION				
		PA	INFUNDIBULAR RV	RV, LOW	FEMORAL ARTERY	
7	6 (e.w.)*	27/4		46/2-4	Normal by cuff	None
9	8 (e.w.)*	19/6		48/5	Normal by cuff	None
39	6	26/11	48/8	51/0-6	115/58	25% L-R
41	8	35/0	45/6	50/0	105/80	None
45	9	35/10	45/0	45/0	110/70	None
47	3	30/14	54/6-12	54/6-12	120/82	None
50	2 wk.	17/7	27/3	33/2	115/70	None

*Catheterization studies done elsewhere.

At all operations, extracorporeal circulation of blood through a modified Gibbon-type pump-oxygenator was employed.[8, 9] The surgical technique used for establishing whole body perfusion has been previously described.[10] The technique of perfusion itself has undergone some changes during the 3 years that these operations were done; since February, 1957, the perfusions have been managed in a relatively standard fashion,[11] employing flow rates of approximately 2.4 L. per minute per square meter of body surface for most patients. Cardiac asystole, induced by the Melrose technique,[12] has been routinely used since August, 1956, beginning with Case 21. The early surgical technique for closure of the ventricular septal defect before the use of asystole has been detailed.[13] Since asystole has been used, the technique basically is the same as that for isolated ventricular septal defect.[14] Prior to Case 15, pulmonary stenosis was treated by pulmonary valvotomy and by infundibular resection of varying degrees of completeness. The use of polyvinyl (Ivalon) sponge in the outflow tract and pulmonary artery[15] was then begun and, in general, the indication for its use in a given case has been that, in the judgment of the surgeon, complete valvotomy and infundibular resection alone would not provide a large enough pathway from right ventricle to pulmonary artery.

Preoperative and postoperative studies of arterial oxygen saturation at rest and during exercise were made for most patients with an ear oximeter. Postoperative cardiac catheterization was done in certain instances. In most patients, measurement and recording of intracardiac pressures were done in the operating room following repair of the defects. Necropsy was performed on all patients dying in the hospital, except one.

HOSPITAL MORTALITY AND FACTORS AFFECTING IT

Mortality.—Twenty-one of the 74 patients operated on died in the hospital, an over-all mortality rate of 28 per cent. The first 5 patients all died, and no further open operations were performed for the tetralogy of Fallot in our institution until the fall of 1955 when use of the procedure was resumed. The hospital mortality in the subsequent 69 cases was 23 per cent. In the last 25 cases there have been 4 deaths, a mortality of 16 per cent. This is probably representative of the present risk, although there have been no deaths in the last 10 cases.

Identification of the cause of death following any operation may be difficult, particularly one as complex as the open repair of tetralogy of Fallot. Table I gives the "probable cause" of death, and some comment of these and other factors related to hospital mortality seems warranted.

Perfusion.—Detailed information concerning the cases in which it was felt perfusion played a role in the fatality is given in a previous article analyzing all deaths related to perfusion.[7]

Degree of Relief of Pulmonary Stenosis as Related to Mortality.—Recordings were made in the operating room of low right ventricular and aortic pressure following repair in 58 of the 74 cases (Table I). Prior to repair in the tetralogy of Fallot, low right ventricular and left ventricular or aortic pressure are identical and pulmonary artery pressure is low. In most cases, pulmonary artery pressure was normal or slightly low after repair, the highest systolic pressure being 44, with a diastolic of 9 mm. Hg (Case 69). When pressure in the inflow portion of the right ventricle was elevated after operation, it resulted from residual pulmonary stenosis. Exact evaluation of the degree of stenosis requires data on flow at the time pressure recordings are made and these are not available in this study.

It seemed helpful to the evaluation of the degree of residual stenosis to plot systolic pressure from low in the right ventricle against that in the aorta (Fig. 1).

In 32 patients, the ratio of low right ventricular systolic pressure to aortic systolic pressure was less than 0.5. It is believed that this ratio is indicative of satisfactory relief of pulmonary stenosis. The hospital mortality was 9 per cent in this group. The ratio was 0.5 or more in 26 patients with a hospital mortality of 38 per cent. This latter group represents surgical failures, not a type of pulmonary stenosis which is inherently uncorrectable.

It is known on the basis of this experience that good relief of pulmonary stenosis can be achieved in about a third of the cases by radical resection of the crista supraventricularis, either alone or with valvotomy, and that in about a third only the *proper* employment of polyvinyl (Ivalon) sponge for enlargement of the outflow tract will suffice. Individual examples of failure and success by these various methods are shown in Figs. 2, 3 and 4. Even the difficult condition with a long, narrow outflow tract, a narrow pulmonary valve ring, and a narrow pulmonary artery can be successfully treated by proper application of Ivalon reconstruction (Fig. 5). This anatomy and thus the need for complete reconstruction are found in the remaining third of the cases.

It is believed that in 7 of the 21 deaths in this series, failure to relieve adequately the pulmonary stenosis was a significant factor in the failure to survive. One additional patient (Case 34) died 6 weeks after returning home from intractable right heart failure which probably resulted from poor relief of the pulmonary stenosis.

Completeness of Repair of Ventricular Septal Defect as Related to Mortality.—Incomplete repair of the ventricular septal defect results in a left-to-right shunt at ventricular level when the relief of the pulmonary stenosis has been sufficient to produce a pressure lower in the right than in the left ventricle.

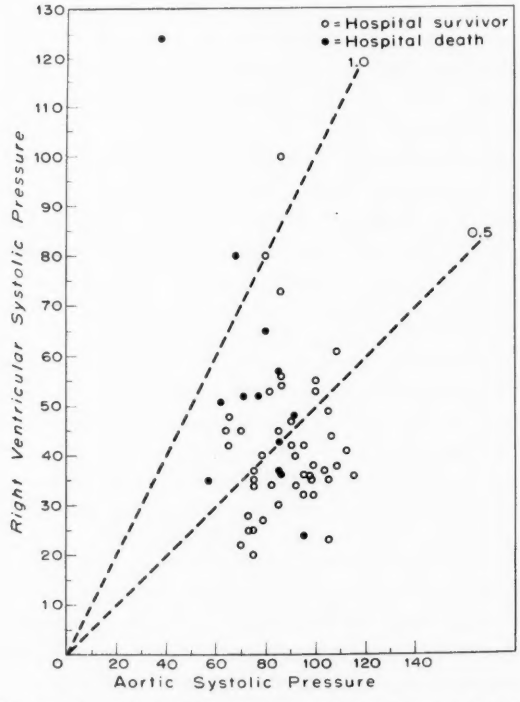

Fig. 1.—Degree of residual pulmonary stenosis as indicated by relation of the systolic pressure in right ventricle to the systolic pressure (mm. Hg) in aorta. Measurements were made in operating room after repair. All cases in which such data are available are included. High right ventricular systolic pressure resulted from incomplete relief of pulmonary stenosis, pulmonary artery pressure being low or normal in all cases.

It is reasonable to believe that this suddenly imposes a strain on the left ventricle and that systemic flow may be impoverished.

In 3 of the 21 patients who died in this series, there was an incomplete repair of the ventricular septal defect. In 2 of these 3, death occurred with progressing hypotension. It appears likely that the incomplete repair of the defect and consequent left-to-right shunt was a significant factor in these fatalities.

Associated Anomalies of the Coronary Arteries Related to Mortality.—Four patients had anomalies of the coronary arteries. In Case 32, a large branch of the right coronary artery crossed the outflow tract of the right ventricle. At operation, the importance of this artery was not recognized and it was divided in making the incision into the right ventricle. The child died at the end of

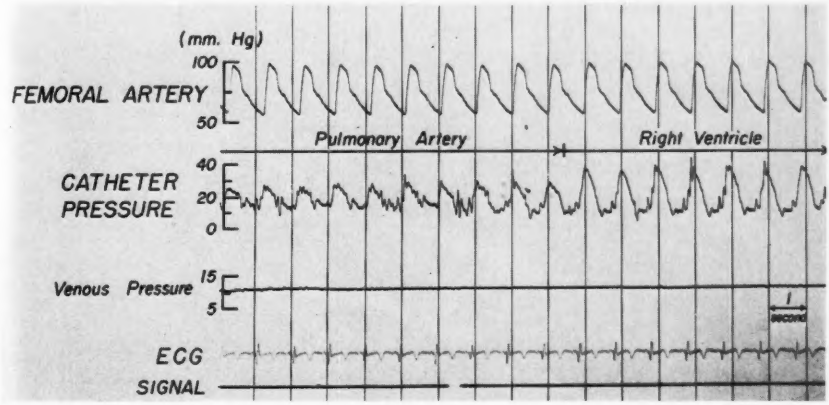

Fig. 2.—(Case 57.) Reproduction of photographic record of intracardiac pressures made in the operating room following closure of ventricular septal defect and relief of pulmonary stenosis by valvotomy and infundibular resection. Pulmonary artery and right ventricular pressures are recorded during withdrawal of the catheter from the pulmonary artery, the catheter having first been inserted through a needle into the lower part of the right ventricle and advanced into the pulmonary artery.

There remains only a 10 mm. Hg gradient in pressure from pulmonary artery to low in right ventricle. This is considered a good result.

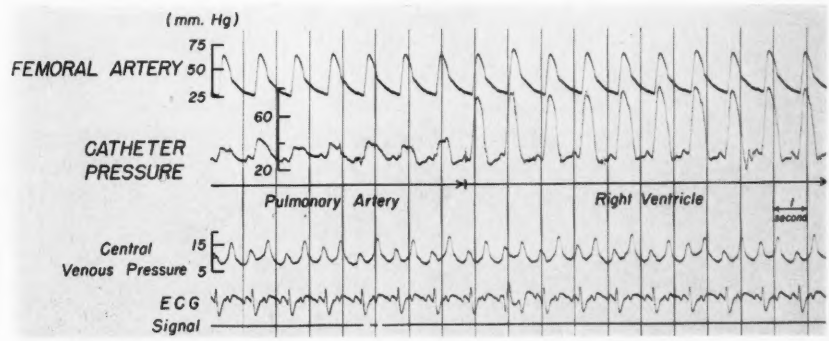

Fig. 3.—(Case 36.) Reproduction of photographic record of pressures recorded as in Fig. 2. Valvotomy and infundibular resection were quite inadequate in this case, since there was a large pressure gradient between pulmonary artery and right ventricle. Right ventricular systolic pressure slightly exceeds aortic systolic pressure. Note elevated central venous pressure, although patient was not hypervolemic as judged by preoperative and postoperative weights. Patient died.

the operation and at necropsy complete absence of the left coronary artery was demonstrated.* Division of the branch of the right coronary artery supplying the left ventricle seems clearly the cause of death.

*For this and the other pathologic studies herein reported, we are indebted to Dr. J. E. Edwards.

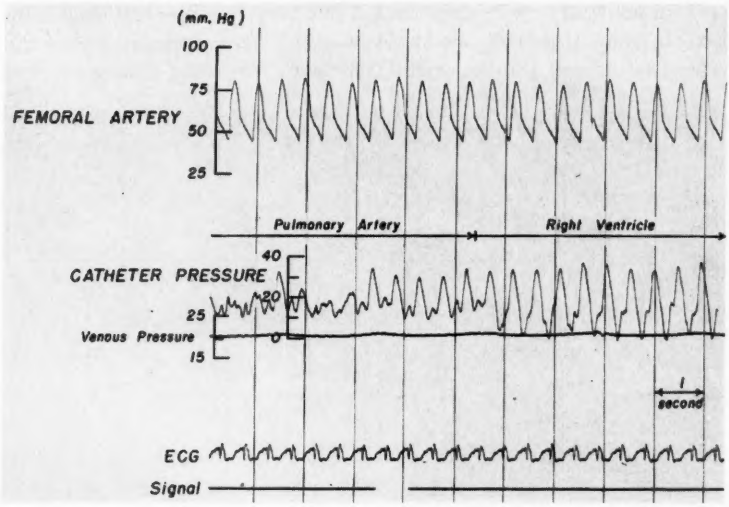

Fig. 4.—(Case 60.) Reproduction of photographic record of pressures recorded as in Fig. 2. Following valvotomy and infundibular resection, the very narrow right ventricular outflow tract and pulmonary valve ring were enlarged by reconstruction with polyvinyl (Ivalon) sponge. The good relief of pulmonary stenosis is demonstrated by the pressures recorded through the catheter during its withdrawal from pulmonary artery to right ventricle.

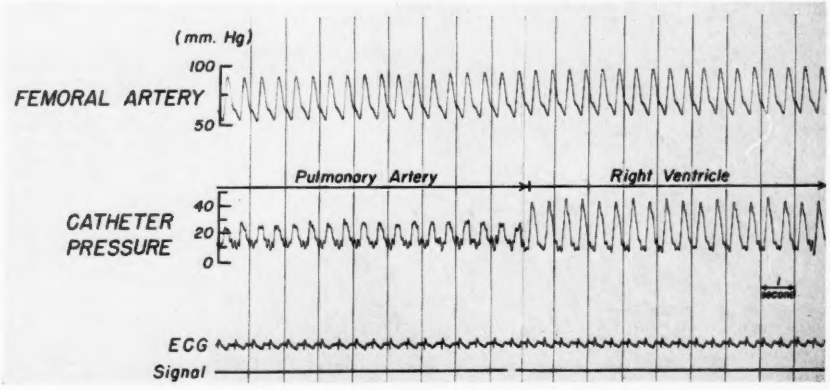

Fig. 5.—(Case 62.) Reproduction of photographic record of pressures recorded as in Fig. 2. Polyvinyl reconstruction was carried to bifurcation of pulmonary artery because of the very narrow outflow tract of right ventricle, narrow pulmonary valve ring, and diminutive pulmonary artery. The residual systolic gradient of 16 mm. Hg between pressures in the pulmonary artery and low right ventricle is considered functionally insignificant.

The lack of appreciable difference between the diastolic pressures in the pulmonary artery and right ventricle is related to the cutting through and Ivalon reconstruction of the pulmonary valve ring.

In Case 44, a large branch of the right coronary artery crossed the outflow tract of the right ventricle to supply the left anterior descending artery. Again, this was divided in the process of entering the right ventricle. The child died 48 hours after operation and the infarct demonstrated low in the left ventricle is considered to be the cause of death.

In the two subsequent patients with this finding at operation, the large anomalous branch from the right coronary artery was preserved. One (Case 52) made an uneventful recovery and the other (Case 56) died, presumably of other causes, since the vessel was patent at necropsy and there was no evidence of myocardial necrosis.

Heart Block as Related to Hospital Mortality.—In 4 of the 21 deaths, complete atrioventricular dissociation in the postoperative period appeared to be a significant factor. One patient (Case 3), treated early in 1955 before supportive care for patients with heart block was well understood, died at the end of the operation. Another (Case 12) was placed on the artificial pacemaker a few hours after operation because of complete heart block which developed during repair of the ventricular septal defect. Adequate cardiac rate and systemic blood pressure were maintained for 10 hours, following which the heart no longer responded. Incomplete repair of the ventricular septal defect and incomplete relief of the pulmonary stenosis probably were also factors contributing to the death.

In Case 28, operation was done in haste because of poor perfusion, and relief of the pulmonary stenosis was inadequate. Complete atrioventricular dissociation was present when the heart resumed its beat after induced asystole, but this had changed to a 2:1 block by the time the incision was closed. Three hours after operation complete heart block was again present, but by then the child's general condition was very poor. She died 3½ hours later. Death had seemed inevitable even before the redevelopment of complete heart block.

The fourth patient (Case 64) died of what was probably heart failure 13 days after operation. It is believed that the complete atrioventricular dissociation which she had may have contributed to the cardiac failure although for the last 11 days of her life the ventricular rate was adequate without the use of an artificial pacemaker.

Left Ventricular Failure as Related to Hospital Mortality.—In the initial report on open intracardiac surgery from this clinic,[16] it was suggested that one patient (Case 1), with tetralogy of Fallot, died because the left ventricle was unable to accommodate itself to the suddenly enlarged pulmonary blood flow and pulmonary venous return.

Following this, left atrial pressure was monitored during operation in a group of patients, and striking elevations were not noted after repair (Table IV). The highest left atrial pressure recorded by us in patients with diminished pulmonary blood flow prior to repair was in a patient who did not have the tetralogy of Fallot. This boy had severe pulmonary stenosis, right ventricular pressure of 200 mm. Hg systolic, and right-to-left shunt across a small

ventricular septal defect. The left ventricle was diminutive. Left atrial pressure after repair was 24/12 with systemic venous pressure being 11 (mean). This patient survived.

Interpretation of the values for pulmonary and systemic venous pressure is difficult without rather exact knowledge of blood volume at the time the measurements are made. In early operations, blood volume was probably not maintained as constant as it has been in more recent operations. However, the values for left atrial pressure in the operating room following repair in these cases do not support a belief that left ventricular failure was present at that time. It is not at present believed that this is the explanation for the death in Case 1.

TABLE IV. LEFT ATRIAL AND SYSTEMIC CENTRAL VENOUS OR RIGHT ATRIAL PRESSURE (MM. Hg) IN OPERATING ROOM AFTER REPAIR OF TETRALOGY OF FALLOT

CASE	LEFT ATRIAL PRESSURE	CENTRAL VENOUS OR RIGHT ATRIAL PRESSURE
7	10/5	16/12
8	17/12	17/12
9	15/8	12/18
10	16/6	24/16
11	8/6	8
12	18/5	18/8
13	14/8	10/7
15	13/7	6/4
16	10/4	11/4
17	8/4	7/6
18	7/4	6
19	14/7	16/11
24	12/6	12/8
65	13/4	18/7
66	15/7	13/7
67	8/1	12/6

Since the first 5 deaths, only one patient (Case 56) has died with frank pulmonary edema. Left atrial pressure was not measured in the operating room in this case. The patient was not hypervolemic and weighed 320 grams less immediately after operation than before. Necropsy disclosed accurate repair of the ventricular septal defect. There was residual pulmonary stenosis. The perfusion had been in all ways standard and satisfactory. This patient had been profoundly handicapped prior to operation. He was not digitalized until after the onset of pulmonary edema which occurred about 4 hours after operation and persisted until death. There was also systemic hypotension which began about 2 hours after operation.

LATE RESULTS

Four of the 53 patients who survived operation and the postoperative period died after leaving the hospital. One (Case 33) died 6 months postoperatively of intractable Pseudomonas bacteremia and presumed bacterial endocarditis, having been operated on during the short period late in 1956 when this complication was occurring in some of our patients.[7]

A 5-year-old boy (Case 38) died at home 8 months after operation; he had been completely normal in all activities and appearance until he became suddenly

ill with cough and respiratory distress and died 6 hours later. Sinus rhythm had been present at all times in the postoperative period and at dismissal. The ventricular septal defect was repaired by direct suture and repair had seemed complete and accurate. The ratio of right ventricular to aortic systolic pressure was 0.6 after repair. Unfortunately, necropsy was not obtained.

Another patient (Case 21) died 2 months after operation with a heart which was shown to be huge by roentgenogram of the thorax taken one week before death. As indicated in Table II, it is believed that grossly incomplete repair of the ventricular septal defect caused his death. In Case 34, death occurred at home of intractable right heart failure 2 months after operation which it is believed resulted from poor relief of pulmonary stenosis.

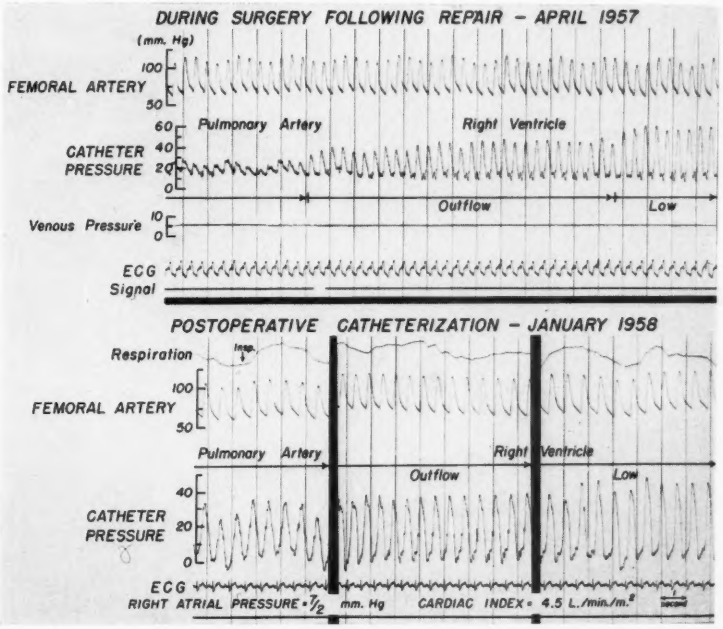

Fig. 6.—(Case 41.) Comparison of pressures in pulmonary artery and right ventricle at operation and 9 months later at cardiac catheterization. Right ventricular systolic pressure is slightly lower 9 months later than it was immediately after the repair. The ventricular septal defect was found to be completely closed at catheterization.

Eleven patients (Case 63 through 74), although well when dismissed from hospital, were operated on too recently to allow evaluation. The remaining 38 patients are enjoying full activity and are completely without symptoms. None is cyanotic at rest or with exercise. This is in clear contrast to the pitiful preoperative status of most of these patients.

Of the 49 surviving patients, 5 are considered to have only fair relief of pulmonary stenosis but are asymptomatic. One operated on recently has had poor relief of pulmonary stenosis. Six have either evidence of or strong possibility

of a small left-to-right shunt at ventricular level which to date has caused no symptoms in 5; the sixth (Case 69) was operated on too recently to allow symptomatic evaluation.

Postoperative cardiac catheterization has been done in only 7 cases. In only one (Case 39) was a residual small shunt demonstrated. In all, relief of pulmonary stenosis was quite satisfactory (Fig. 6).

PRESENT METHODS OF MANAGEMENT BASED ON THESE EXPERIENCES

Selection of Cases for Operation.—No patient with the tetralogy of Fallot is considered to be too ill for operation and a previous operative procedure is not considered a contraindication for operation. One surviving patient (Case 42) had had two previous operations; once a Potts anastomosis had been performed and, the second time, infundibular resection. Five other patients had

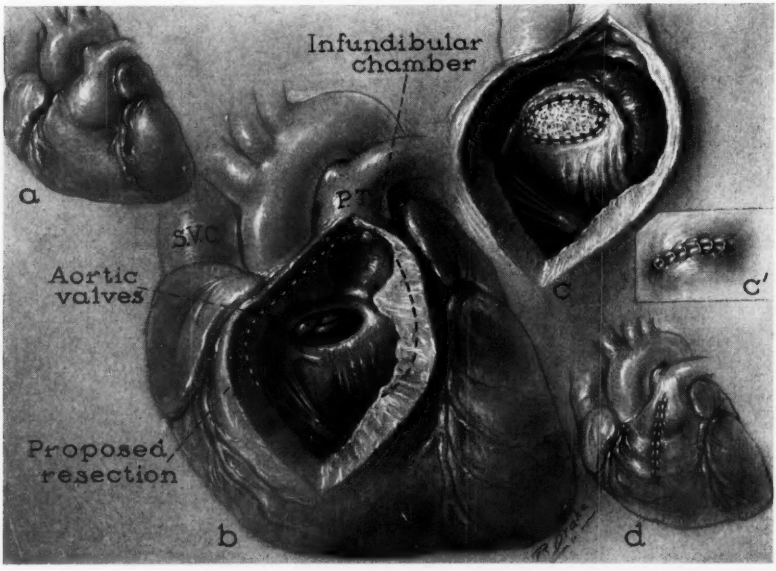

Fig. 7.—Open intracardiac repair of tetralogy of Fallot with infundibular chamber and wide pulmonary valve ring and artery. The unopened heart (*a*). The first step, after induction of cardiac asystole, is wide excision of the hypertrophied crista supraventricularis and relief of the infundibular pulmonary stenosis (*b*). Pulmonary valvotomy is performed when indicated. The ventricular septal defect is then repaired by direct suture (*c'*) or with compressed Ivalon sponge (*c*). If careful examination discloses a now adequate pathway through the outflow tract and pulmonary valve ring and artery, plastic reconstruction is not necessary and the ventriculotomy is closed (*d*).

undergone previous Blalock anastomoses. One other deeply cyanotic patient, not included in this report since she proved at operation to have atrial septal defect and pulmonary stenosis, previously had undergone a Blalock operation. Two of these 7 patients with previous anastomotic procedures died after operation, which included closure of the previously created shunt, one being the first one operated on in this series (Case 1) and the other (Case 14) dying from incomplete repair of the ventricular septal defect. The other 5 are well.

Perfusion.—Accurate and complete intracardiac repair of the tetralogy of Fallot is time consuming in our hands. Thirty to 40 minutes of induced cardiac asystole and a total perfusion time of 40 to 70 minutes are usually required. In order that there be little or no mortality referable to the perfusion, it is believed that it must be conducted in an optimal way.[7] In the operations done in this series in the last 12 months, no deaths have been considered related to the perfusion.

The large bronchial flow and consequent large intracardiac return necessitates an adequate intracardiac sucker system as a part of the pump-oxygenator employed. In all these cases, the system utilized[17] has allowed safe admittance of the aspirated blood to the general venous return and good visualization of the operative field.

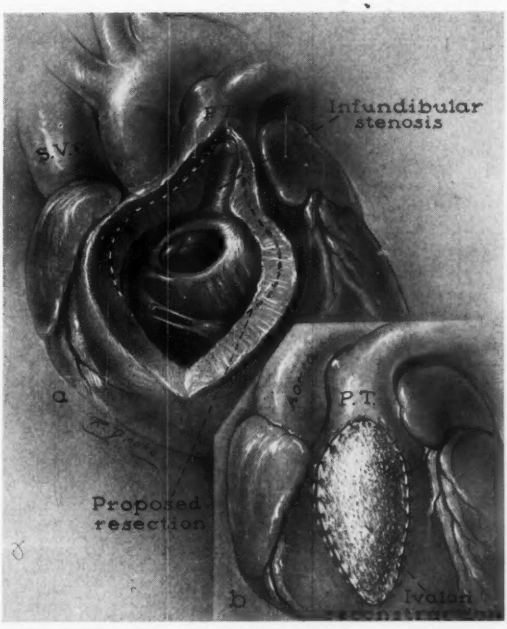

Fig. 8.—In cases without an infundibular chamber and with the infundibular narrowing going to the valve ring, infundibular resection (*a*) usually does not result in a sufficiently wide pathway. In such cases, curved compressed Ivalon sponge is used to effect a plastic reconstruction and enlargement of the outflow tract (*b*). When the pulmonary valve ring is narrow, the incision and reconstruction is carried across the ring.

Operative Technique.—The details of the surgical technique at present considered advisable for repair of the tetralogy are illustrated in Figs. 7, 8, and 9. Accurate visualization and repair of the ventricular septal defect are accomplished in a fashion similar to that for isolated ventricular septal defect.[14] An Ivalon sponge prosthesis is often employed for repair of the ventricular septal defect, although recently direct suture has been more commonly employed. In nearly all cases, infundibular pulmonary stenosis necessitates resection of the limbs of the crista supraventricularis. Pulmonary valvotomy is accomplished where there is valvular pulmonary stenosis.

In light of the apparent relation between the adequacy of relief of the pulmonary stenosis and mortality, it is important to evaluate the cross sectional area of the outflow tract of the right ventricle, pulmonary valvular ring, and pulmonary artery. If it is clearly adequate for the accommodation of normal flow with minimal pressure gradient between the sinus portion of the right ventricle and the pulmonary artery, nothing further is necessary. If not, plastic enlargement is effected by the insertion of a curved, compressed, Ivalon sponge.

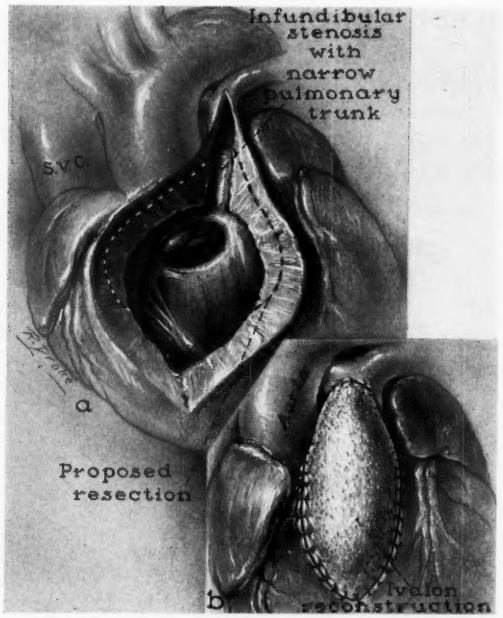

Fig. 9.—A very narrow main pulmonary artery, or trunk, is sometimes present along with a narrow pulmonary valve ring and right ventricular outflow tract. After infundibular resection, the incision must be carried to the bifurcation of the pulmonary artery and plastic reconstruction and enlargement of the *entire* area affected. Note that the compressed Ivalon sponge is convexly curved to enlarge the cross sectional area beneath it.

Induced cardiac asystole is considered essential to accurate repair. It is probably important to abandon it after 40 minutes, leaving, if necessary, reconstruction of the outflow tract to be done with the heart beating. With the use of asystole, adequate exposure for the intracardiac manipulations can be obtained through a relatively small incision placed mostly in the outflow tract of the right ventricle. This may be advantageous with regard to cardiac function in the postoperative period.

Associated lesions, such as atrial septal defect or patent ductus arteriosus, must be identified and repaired. Where there is a large anomalous branch of the right coronary artery, decision as to procedure is difficult. It appears unwise to sever it. In such a case, if good relief of pulmonary stenosis is possible without a plastic reconstruction of the outflow tract, the operation should proceed as

planned, extending the incision only up to this vessel. If adequate relief of the pulmonary stenosis is impossible to achieve in this fashion, the plans for proposed complete intracardiac repair probably should be abandoned and either isolated infundibular resection or an anastomotic procedure performed.

Postoperative Care.—Administration of fluid is managed as in other cases after intracardiac surgery.[18] Patients are kept in an oxygen tent with a humidified atmosphere for 48 to 72 hours after operation. The most important decision to be made concerns administration of digitalis. It is believed not advisable routinely to bring these patients to surgery digitalized, nor routinely to administer digitalis in the postoperative period. When the pressure low in the right ventricle remains moderately elevated after repair, digitalization on the day of operation has proved beneficial. Also, should hypotension or evidence of pulmonary edema develop, digitalis should probably be administered.

Many patients are not digitalized in the early postoperative period and, in some of these, retention of fluid and hepatomegaly insidiously develop and become apparent 10 to 14 days after operation. Restriction of salt and digitalization are instituted and maintained for 4 to 6 weeks, following which no further difficulty has developed.

When complete atrioventricular dissociation and slow ventricular rate have occurred, isoproterenol hydrochloride (Isuprel) and the artificial pacemaker are employed as they are after repair of isolated ventricular septal defect. Properly managed, heart block should rarely be a cause of death in the hospital.

SUMMARY

Experiences with open intracardiac repair for the tetralogy of Fallot are described together with details concerning the factors contributing to hospital and late mortality. The operation, perfusion, and postoperative management must be done with precision if the best results are to be obtained.

The excellence of the late results and the reasonable although significant operative mortality render open intracardiac repair an effective treatment for the tetralogy of Fallot. A longer follow-up of a larger series of cases will be required finally to establish whether it will replace all other operations for this lesion. Yet it is, in the opinion of the authors, at present the treatment of choice.

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DISCUSSION

DR. RICHARD A. RASMUSSEN, Grand Rapids, Mich.—We all admire the results obtained in the successful case of tetralogy of Fallot when corrected by the direct anatomic method. This is the condition which Dr. Blalock first treated successfully in 1945. Dr. Kirklin and his co-workers at the Mayo Clinic are to be commended for this presentation. It is recognized that true anatomic correction is our aim but this cannot always be attained in the problem of decreased blood flow. It must be remembered that there are other far less hazardous procedures which do give a good physiologic result, and these may still be considered for certain selected types of cyanotic heart disease, especially when the risk is great.

In the April issue of the JOURNAL OF THORACIC SURGERY, Dr. Sanger and his associates of North Carolina suggested the use of a vena caval-pulmonary artery anastomosis to increase the pulmonary blood flow. This procedure would also decrease the work load of the right heart. They presented experimental data indicating the feasibility of the procedure. I and my associates would like to report the use of a superior vena caval-pulmonary artery anastomosis for transposition of the great vessels with pulmonary stenosis. This was done in a 17-month-old boy who at 4 months of age began to have severe cyanosis with episodes of unconsciousness. These spells became more severe and frequent over a period of one year, until he was admitted to Blodgett Memorial Hospital for diagnosis and treatment, having been in oxygen for one month. Consideration was

given to the various shunting procedures that might be done on this child. On exploration on April 24, 1958, the anatomic findings and additional pressure studies confirmed the diagnosis of transposition and pulmonary stenosis. It seemed that a superior vena caval-pulmonary artery shunt would be ideal for this patient, and this was done.

(slide) This is an x-ray photograph which demonstrates the shape of the heart, the decreased pulmonary vasculature, and the aorta which arises from the right ventricle, and the pulmonary artery probably arising from the left ventricle.

(slide) This is a sketch showing the findings at operation as described. Note the transposition and the pulmonary stenosis. We simply disconnected the superior vena cava from the right auricle and connected it directly to the disconnected distal end of the right pulmonary artery after the latter had been severed at its origin from the main pulmonary.

(slide) This is the result one week later. Note the good color.

The immediate result of this procedure seems to be excellent. The increased oxygen saturation changed from preoperative catheterization values of 59 per cent to 83 per cent immediately following surgery. The color improved immediately. It should be pointed out that the superior vena cava blood bypasses the right heart completely and therefore eases the work of the heart. The increased blood flow through the right lung undoubtedly accounts for the increased oxygen saturation and the clinical improvement. The procedure was well tolerated in a poor risk case. The operation is essentially a continuous perfusion of the right lung. It has a real advantage over the other shunting procedures in that the strain on the heart is decreased instead of increased.

From the success in this case it would appear that the physiologic studies of Sanger and associates are confirmed in the human being. It is hoped that others will consider and try this new shunting technique for poor risk cases similar to the one reported, and other similar problems of decreased pulmonary blood flow.

DR. FRANK L. GERBODE, San Francisco, Calif.—I want to speak of one point Dr. Kirklin made about the left-to-right shunt which results after reopening of a septal defect following repair of a tetralogy of Fallot. We have operated upon 14 patients now with tetralogy of Fallot and we have 10 living. Three patients died because of difficulty with outflow tract problems, and I must confess we were not as good as Dr. Kirklin was in taking care of them. I wish particularly to speak of one patient, an adult, who had a tetralogy of Fallot. He had a perfectly adequate operation, we thought, with reaming out of the outflow tract and repair of an interventricular defect with an Ivalon prosthesis. On about the tenth postoperative day, it was quite obvious that the interventricular defect had opened. That resulted in a truly colossal left-to-right shunt. The calculated shunt flow was something like 30 L. in this boy. He developed an enormous heart, a gallop rhythm, and all the evidence of acute heart failure. It seemed as though far more blood passed through the shunt than one might expect from a defect of this size. The flow suggested that some mechanism was not present in the lungs, which might have been present in an ordinary interventricular defect; a mechanism which perhaps protects against a flow of this magnitude under such circumstances. In any event, after a month we took the boy back to the operating room and found that the Ivalon prosthesis had separated on one side. We were fortunately able to close it successfully and I am glad to report that he is well. But I must say that the second operation, after a month, was fraught with certain difficulties, because enough time had elapsed to vascularize the adhesions, and hemothorax and hemocardium required another operation. After the experience in this case, and in one other, I would suggest that if failure is evident, perhaps an earlier intervention at 2 or 3 weeks might be indicated.

SIR RUSSELL C. BROCK, London, England.—In the very short time available for discussion it is impossible to do more than make straight comments and observations without supporting argument.

Even after the magnificent papers we have listened to I do not think the problem of the so-called corrective treatment of Fallot's tetralogy has been settled. We are told that the complex problems of the smallness of the pulmonary outflow tract can be solved by sewing a large piece of plastic material either into the wall of the infundibulum or, even more disturbing, across the pulmonary valve ring and into the wall of the pulmonary trunk. This procedure has several grave disadvantages and I feel we are in danger of being misled by the brilliance of the pure technical achievements now permitted by successful "heart-lung bypass," we are in danger of ignoring certain fundamental surgical principles which, I feel, cannot be ignored.

The introduction of foreign substances into the body is rarely acceptable, safe, or satisfactory as a long-term policy. A piece of inert material buried in some relatively inactive part of the body may give no trouble. But here it is proposed that it is safe, and is sound surgery, to introduce foreign material into one of the most active parts of the body—the outflow tract of the right ventricle. Moreover, in one third of the cases this substance is astride the pulmonary valve which is thereby rendered totally regurgitant. I find it difficult to believe that a foreign substance, constantly exposed to such severe mechanical strains, will not give rise eventually to serious trouble. This is quite apart from the inevitably harmful effects of total pulmonary regurgitation.

This technique also ignores the fact that the disproportion between the two circulations is more extensive than the pulmonary outflow; it extends to the balance of power and distribution of effort of the two ventricles.

I find it difficult to believe that this technique is an acceptable solution to the problem of the correction of the smallness of the pulmonary outflow tract.

I suggest that there is an alternative method of increasing the size of the outflow tract more physiologically, that is by giving nature a chance, by encouraging the natural process of growth. This process is inevitably related to function and can be achieved by a preliminary direct operation to relieve the pulmonary stenosis, whether it be valvular or infundibular or both. When sufficient time has elapsed to enable the pulmonary outflow to develop and the balance of the ventricles to be more happily adjusted, then the septal defect can be closed by a second stage.

I am second to none in agreeing that, whenever possible, a single-stage, totally corrective operation should be done for Fallot's tetralogy. Fallot's tetralogy, so-called, is, however, not a disease entity, is not a homogenous group. The label covers a whole range of conditions of abnormal development, and to apply one standard method of operation to all seems to lack finesse. I believe that for these very difficult types of Fallot's tetralogy in which the pulmonary outflow is so small and the disproportion between the aorta, the pulmonary vessels, and the two ventricles is so extensive that some form of two-stage operation is necessary, the first, or preliminary stage should relieve the stenosis; the second stage will consist of closing the septal defect.

Time alone can tell whether a standard one-stage corrective procedure is possible. Because these patients leave the hospital apparently well does not convince me that they will continue well for the remainder of the long life that should lie before them if they have in truth been "totally corrected and cured." I leave to you the simple thought that in some of these cases there is and will always be a place for some form of two-stage, gradually corrective procedure.

DR. WILLIAM W. L. GLENN, New Haven, Conn.—I would certainly like to express my very great admiration of Dr. Kirklin's and Dr. Lillehei's magnificent work in the correction of the tetralogy of Fallot. The direct correction of this lesion is obviously the procedure of choice when possible. We have been interested in the problem of the occasional case of the tetralogy that cannot be corrected by the direct procedure and, particularly, in other patients with conditions characterized by malfunction of the right side of the heart where correction by direct technique is either not possible or is unsatisfactory.

About 3½ years ago, in 1954, we reported our first experience with the application in the experimental animal of a procedure similar to that just described by Dr. Rasmussen. A shunt was made between the superior vena cava and the distal right pulmonary artery. After extensive experimental trial, this operation was applied to a patient with a single ventricle pulmonary stenosis in transposition of the great vessel (slide). This slide shows an angiogram of a child 7 years of age who had this combination of defects and where the distal end of the right pulmonary artery was anastomosed to the side of the superior vena cava and the superior vena cava was then ligated just above the right auricle. This angiogram was made 2 months following operation, which was done in February, 1958. It shows the dye injected into the left brachial vein entering the superior vena cava, then the distal right pulmonary artery bypassing the right side of the heart. The dye then passed rapidly through the lung, the pulmonary veins, and into the left auricle.

I would like to point out particularly that this procedure is fraught with great hazard if thrombosis of the anastomosis should occur. It should therefore be done only in preference to other corrective or palliative procedures where the indications are exceptionally clear. I should like to emphasize, also, that the procedure should not be performed unless the pulmonary artery pressure is low or certainly normal, but never where it is elevated, and it should be performed only when the vessels concerned, the pulmonary artery, and the superior vena cava, are of large size.

DR. C. WALTON LILLEHEI, Minneapolis, Minn.—Tetralogy of Fallot is a curable malformation! Our experiences of the past 4 years demonstrate that unequivocally. Moreover, the complete correction can be carried out in consecutive patients unselected other than by virtue of the fact that they are "in trouble," with an immediate operative risk comparable to and even less than that possible with the palliative procedures. And, beyond this, it is in the months and years following operation that the great dividends of restoring the circulation to normal are returned with compounded interest.

In the beginning in 1954, due to the learning phases inherent in the development of both new perfusion methods as well as new operative techniques for a complex defect, the immediate operative risk was higher for the complete correction than for the palliative procedure. However, even then this increased risk was more apparent than real for, in the first 10 patients to have the curative procedure, there were six successes and four deaths (Ann. Surg. 142:418-445, 1955). In the 3½ years that have elapsed since this first series was treated there has been no late mortality among the successful cases and, in fact, none of these 6 patients has had any cardiac difficulty whatsoever. Most have now been restudied objectively and proved to have normal physiology. Thus, even this initial mortality of 40 per cent compares quite favorably with the 30 per cent death rate noted in a series of 110 shunted patients followed 2 to 10 years (Arch. Surg. 75:928-945, 1957). Moreover, in this latter series an additional 16 per cent were alive but unimproved and obvious candidates for another operation.

Therefore, at the present time, when the curative procedure can be carried out with an operative risk of 10 per cent or less and the late mortality can be expected to be negligible, there is not the slightest doubt as to the procedure of choice.

As a result of this and numerous other therapeutic gains, the field of intracardiac surgery is a burgeoning speciality. The transition from extracardiac to intracardiac techniques requires not only broad operative experience in thoracic surgery but a dedicated interest and knowledge as well of the known and experimental aspects of the physiology of respiration and circulation, not to mention cardiology. Thus, no wonder one finds now and then traces of doubt expressed by some surgeons beset with early failure. However, this lack of courage upon their part to carry through can be expected to pass.

At the 1958 Meeting of the University Surgeons in February, we sought to analyze our experiences in the surgical treatment of the first 100 patients with the cyanotic variety

of tetralogy and five factors stood out as important contributions to the significant reduction in risk which has occurred. I should like to show this slide which summarizes these as follows:

1. *Efficient Perfusion.*—Our average cyanotic tetralogy patient requires a 60-minute perfusion for a curative operation. Arterial blood pressure is continuously monitored and is maintained at a normal level by adjusting the flow rate accordingly. Here, in respect to pressure maintenance, is one of the values of using an occlusive pump. Hemolysis, as Dr. Hodges has pointed out in the Forum, has virtually nothing to do with whether a pump is occlusive or nonocclusive, but maintenance of flow against resistance does.

The metabolic efficiency of the helix reservoir bubble oxygenator has been an important factor contributing to routine success in these longer perfusions. Especially important are its safety factors related to sterilization of all parts in contact with blood by autoclaving, and the fact that the entire extracorporeal circuit except for a few easily cleaned stainless steel connectors and adaptors is disposable. It is surprising to me that in 1958 some surgeons are still working with equipment that cannot be heat sterilized and is not only *not disposable* but of design difficult to clean. In addition, some of the film oxygenators in use require significant quantities of saline, albumin, dextran, or P.V.P. in order to function. It is no wonder then that, under such circumstances, patients are lost due to such complications as infection, hemorrhage, and pulmonary or cerebral edema.

Moreover, gadgeteers obviously with more money than physiologic background are still equipping pump oxygenators with various electronic level sensing devices that, in situations of duress, function solely to maintain the machine's blood volume at the expense of the patient's. Nothing could be more ill conceived.

2. *Ventricular Defect Closure.*—In tetrad patients, a prosthesis is necessary very frequently. The defects are usually large and their margins of soft, red muscle will not hold stitches for long under any tension.

3. *Right Ventricular Outflow Tract Reconstruction.*—The severity of the stenosis is widely variable as must be the surgical techniques to relieve it. However, in the severe cases the sine qua non of success is the use of an outflow roof as previously described (Arch. Surg. 73:526-531, 1956). In a few very severe hypoplasias of the bulbis cordis region, it is necessary to continue the outflow roof across the annulus into the main pulmonary artery.

4. *Selective Cardiac Arrest.*—Elective asystole with potassium citrate has proved very valuable in the tetrad group, but must be used *selectively* for best results. That is, induced only if necessary in that particular case and, then, only for as long as absolutely necessary. The duration of arrest is best kept under 30 minutes. We used to vent the left atrium with a catheter in all tetralogy patients (Extracorporeal Circulation, Springfield, 1958, Charles C Thomas, publisher, pp. 41-56) but this is now accomplished by the simpler method of releasing the aortic clamp early enough to allow the ventricular defect itself to act as a vent while the ventricular patch is being seated and the stitches tied.

5. *Complete Heart Block.*—In the present state of our knowledge it has been impossible to avoid this complication in 10 to 15 per cent of tetralogy patients. Surgeons who say they have no heart block problem are simply not doing much surgery of this type. Fortunately, the myocardial electrode with internal pacemaker stimulation handles the situation very well until sinus rhythm returns or adaptation to the slower rate has occurred. The next advance is to learn how to avoid block completely.

DR. KIRKLIN (Closing).—I should like to thank Dr. Rasmussen and Dr. Glenn for giving us their experience and their views on this subject. Perhaps I might be permitted to comment specifically on Dr. Gerbode's discussion and that of Sir Russell Brock. It is pertinent I think to emphasize again what Dr. Gerbode has said, namely, that if one relieves the obstruction to outflow from the right ventricle by a reasonably good operation, and leaves the ventricular septal defect open, the residual shunt does not continue to be right-to-left, but becomes, suddenly and overwhelmingly, left-to-right. I think this is obvious. Along the same line one must remember that if one makes a complete repair

of the ventricular septal defect there is suddenly a markedly increased pulmonary flow. In other words, the right ventricle is now ejecting all its blood across the pulmonary valve, whereas prior to that, of course, it was ejecting a good deal of it across the ventricular septal defect. The right ventricular pressure is a function not only of that resistance but also of the flow, and when flow goes up an opening which has been only moderately increased in size by the operation it may produce a right ventricular pressure which is the same as it was before surgery, or indeed higher. So one must open this area widely.

I was privileged to discuss a month or so ago with Sir Russell Brock this problem of the outflow tract, and I think his comments and his admonitions must be very carefully considered. Personally, I agree completely that any foreign substance anywhere in surgery is undesirable and should be avoided if possible. I suppose I am particularly concerned about something like compressed Ivalon sponge, which is fairly leathery and which probably is not incorporated within tissues.

I agree that it might not be a very important technical point whether one repairs the ventricular septal defect by direct suture or sponge, but if both are equally satisfactory then it must be better without a sponge since we have no foreign material. In the outflow tract, however, it appears necessary in some cases to make some sort of plastic reconstruction. I suppose then we must accede to the possible objection that this is the Achilles' heel of this particular operation. Still, we have no evidence as yet, as Dr. Lillehei pointed out, after 2 years of experience, that any one of these patients has had late trouble. One thing that perhaps worries me a bit about a two-stage procedure as suggested by Sir Russell, is whether the very small fibrous pulmonary valve ring, not the outflow tract, not the main pulmonary artery, but this very small ring, would enlarge significantly with the resection of the fibrous tissue beneath it. Perhaps it will, I do not know. I think we have to admit that this is not yet a completely settled point, but I do think we have a right to assert that in the 2 years at least that these patients have been followed there have been no ill effects.

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ATRIAL SEPTAL DEFECT, SECUNDUM

An Analysis of One Hundred Patients Undergoing Open Surgical Repair

Henry Swan, M.D., Allan B. Kortz, M.D. (by invitation), D. Hywel Davies, B.M., M.R.C.P. (by invitation), and S. Gilbert Blount, Jr., M.D. (by invitation), Denver, Colo.

OUR TOTAL experience with the open repair of interatrial septal defects of the so-called secundum variety is now somewhat in excess of 100 cases. In addition, we have treated 20 patients with pulmonary valvular stenosis, associated with patent foramen ovale or atrial septal defect, and a few others with septum primum or atrioventricularis communis. Because of the important differences in the pathologic anatomy and physiology which occur in the presence of these latter anomalies, it seemed wise to confine the subject of this report to a study of those patients who had some variant of the secundum-type lesion, and who did not have pulmonary outflow obstruction. This paper, therefore, concerns the first 100 consecutive patients recommended for surgery and proved to fit into this category at open-heart operation.

SURGICAL BACKGROUND

The history of the operative repair of atrial septal defect has been typical of the recent rapid development of cardiac surgery in general. Groupings for usable techniques and tolerable cardiac manipulations were made in the experimental laboratories after the methods for thoracic exploration in general became understood. Attempts to create an experimental preparation which simulated the clinical defect were soon successful and, using this preparation, actual methods for closed, or nonvisual, repair were soon elaborated. Some of these were crude while others became more refined and, in fact, are still in use today in a few centers. Meanwhile, the effort to develop techniques for the visualization of operative fields inside the heart was vigorously pursued in many laboratories. The first method for open-heart surgery to achieve a degree of safety which warranted application to the human was hypothermia.

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Aided by grants from the United States Public Health Service and The American Heart Association.

Read at the Thirty-eighth Annual Meeting of The American Association for Thoracic Surgery at Boston, Mass., May 16-18, 1958.

and for 3 years before the use of cardiopulmonary bypass became generally available, we gained experience with this technique and solved many of the problems encountered in the open operative repair of atrial septal defect. At present, then, widespread trial of both hypothermia and cardiac bypass is being made in various centers throughout the world. Since by the time the heart-lung machine became available, hypothermia had been developed in our clinic to a degree of safety approaching a risk of zero, and since the operation had proved so effective, we saw no reason to discontinue this method. In the long run, the choice of technique will emerge in terms, first, of safety to the patient and effectiveness of the operative procedure, then, of simplicity, cost, and blood banking problems. In the present series, all of the operations were performed during circulatory arrest while the patient was in a state of hypothermia.

The first studies contributing to the story outlined above are those which evolved a technique for the temporary interruption of blood flow through the heart. It is surprising that this method, first described experimentally by Haecker[1] in 1907, was apparently not used clinically until Swan, in 1949, applied it to the open removal of foreign bodies in the heart[2] and the closed repair of atrial septal defects.[3] Haecker's work was soon confirmed by both Sauerbruch[4] and Rehn.[5] It was soon established by Laewen and Sievers[6] that, in rabbits, inflow occlusion was much better tolerated than outflow occlusion. Survival roles following various durations of inflow occlusion in animals at normal temperatures have gradually become established, and the concept of a rapidly rising mortality after a short safe period has emerged. As a result of experiments by Scheppelman,[7] Carrel,[8] Tuffier,[9] O'Shaughnessy,[10] Adams and Escudero,[11] Shaw and co-workers,[12] Templeton and Gibbon,[13] Cohen,[14] and Swan[15] and their associates, it became apparent that all dogs will survive 1½ minutes of occlusion; most dogs will tolerate 5, whereas the majority will succumb if the period is lengthened to 10 minutes.

Various measures to increase the safety of long- or middle-range occlusion have been suggested. Brain perfusion[6, 10] was not successful. Hyperventilation[14] before occlusion and hexamethylamine[16] were suggested but not widely adopted. Adams and Escudero,[11] in their important study, felt that a gradual return of work load to the heart following occlusion in the middle range helped reduce the incidence of cardiac death. They demonstrated that more blood returned to the heart via the inferior vena cava than via the superior vena cava; occlusion of the former alone caused a 60 per cent drop in carotid artery pressure, while occlusion of the latter caused only a 30 per cent drop. They recommended, therefore, release of the superior vena cava first, followed after a few minutes by release of the inferior vena cava. Thus, the overdistribution caused by a sudden large flow of blood presented to the hypoxic heart is prevented.

The influence of hypothermia on the tolerable limits of inflow occlusion has been extensively studied and the reports are too numerous for review

in this paper. In spite of these studies, however, there is still no general agreement concerning the survival limits in man for the brain and for the heart during cardiac inflow occlusion at various levels of decreased body temperature. Nonetheless, it is apparent, both experimentally and clinically, that hypothermia has lengthened the "absolutely safe" period of inflow occlusion by a sufficient amount to be eminently practical for intracardiac procedures not exceeding 10 minutes in duration.

The development of a method for the experimental creation of interatrial septal defects was an important preliminary to the evolution of techniques for repair. Simple incisions and small excisions of atrial septum promptly heal (Martin and Essex,[17] and Dodrill[18]). Blalock and Hanlon[19] created a persistent defect, but one which lay anatomically above and posterior to the usual clinical lesion. Using the inflow occlusion principle, Swan[15] created large defects in the mid-septum by direct-vision excision. These defects allowed the elaboration and evaluation of techniques for closure. Other methods for creation of the defects were subsequently devised (Hufnagel and Gillespie,[20] Donald,[21] and Gross[22] and their co-workers) and from these studies techniques for closure were suggested.

The first experimental attempt at repair of an atrial septal defect, however, was that of Cohn in 1947,[23] using a patch of auricular wall. Swan,[15] in 1950, suggested the inversion of the auricular appendages through the defect, thus attempting to plug the hole. Although this was only partially successful, a principle was established which later proved of importance. This was the concept of the "doughnut-lumen" of the auricles, which it was shown did not interfere with the flow of blood from the venae cavae to the tricuspid valve. This principle was applied clinically in 1950, and on May 6, a 9-year-old patient was operated upon, using this technique, at the Colorado General Hospital. It is believed that this patient is the first individual to survive an attempt at surgical repair of an interatrial septal defect. (He has subsequently had successful open closure of the residual defect.) The principle of the "doughnut-lumen" was later utilized by Bailey and his colleagues in 1952,[24] who modified the technique to involve suture of the lateral wall of the auricle rather than the appendage, and by Shumacker and his associates,[25] who added to the procedure a sac made of pericardium or plastic materials attached to the auricular wall.

Meanwhile, another variation of the patch idea of Cohn was being explored. Instead of a part of heart muscle, inert plastic buttons were examined to see if they would not excite undue thrombosis and to determine their fate when sutured to the wall of the auricle. Hufnagel and Gillespie, in 1951,[20] described an ingenious method for the application of two nylon buttons. Swan and Stewart, in 1953,[26] described a modification of the original "button" technique which left a polyethylene sheet over the defect inside of the right auricle and, in this publication, described the remarkable process which first covered the plastic with fibrin and then, by the process of endothelization, converted the fibrin envelope to a smooth glistening membrane completely surrounding the polyethylene prosthesis. Later, Donald and associates,[27] using

polyvinyl sponge, Miller and co-workers,[28] Pomeranz, Watkins and Gross,[29] and Bahnson and Baker[30] studied a variety of tissues and plastic materials implanted in the heart. These experiments demonstrated the important fact that, whereas pericardial grafts or other autogenous or homologous free tissue grafts excite thrombosis and are replaced by fibrous scars, a variety of plastic materials are well tolerated in the lumen of the auricle, and excite processes which result in their becoming completely encased in a smooth, endothelized membrane. Utilizing this principle, Kirklin and co-workers[31] reported a successful clinical series, in 1955, placing the polyvinyl sponge across the defect by means of the Gross "well."

Another technique for the closure of septal defects, namely, a circular suture passed outside of the heart around the defect, was suggested by Murray in 1948,[32] and subsequently developed by Söndergaard[33] experimentally, and given clinical trial by Björk and Crafoord.[34] A large suture, in this technique, is passed through the upper edge of the ventricular septum or the lower portion of the atrial septum and then tied down in a previously developed plane between the right pulmonary veins and the posterior aspect of the right atrium, thus squeezing closed the entire atrial septum. It is obvious that this technique, while possible for the simpler defects, is not anatomically suitable for the more complex lesions with aberrant pulmonary veins.

Meanwhile, a direct-vision attack, in 1953, was achieved first by Lewis and Taufic[35] after considerable experimental work in the laboratory utilizing hypothermia, a principle of inflow occlusion and open atriotomy with direct suture of the defect. Shortly thereafter, we also undertook a study of this method[3] clinically, and this report comprises our observations on the use of this method in our first 100 patients treated in this fashion.

ANATOMY

The embryology of the atrial septum has been so well described by Rokitansky[36] and by Patten[37] that the terminology has been universally adopted. In the latter's opinion, the septum secundum defects result from either normal development of the septum secundum with excessive resorption of the valvula foraminis ovalis, or arrest in the development of the septum secundum with failure to reach the caudal margin of the ostium secundum. A further degree of classification would have some clinical merit if it helped the surgeon understand the variations of the anatomy encountered. Kirklin,[31] Lewis,[38] and Bedford[39] and their co-workers have discussed this problem. Our own classification is in general agreement with all three authors, but differs from other systems in our distinction between so-called "primum" defects and atrioventricularis communis. This classification follows.

I. Interatrial septal defect, secundum.
   A. Foramen ovale defects.
      1. Foramen ovale open due to defect in valvula foraminis ovalis, which may be partially present as a caudal or dorsal margin, or as a fenestrated membrane.

2. Valvula foraminis ovalis absent; lower margins apparently continuous with valve of inferior vena cava. Anomalous pulmonary venous drainage may be associated with this defect.

B. Septum secundum defects (high).

These defects are situated immediately inferior to the entrance of the superior vena cava; they usually have no cephalic or dorsal margins; they are often associated with anomalous return of pulmonary veins from the right lung to the right atrium or superior vena cava, or with anomalous pulmonary venous return from the left lung into a left superior vena cava and/or a coronary sinus.

C. Combined defects.

II. Interatrial septal defect, primum.

These defects, which are very rare, are situated in the lower portion of the septum; there is no inferior margin above the upper edge of the ventricular septum, *but also there is no defect or cleft in either of the atrioventricular valves.*

III. Atrioventricularis communis.

1. The atrioventricular cushion is intact and the "ventricularis" part of the defect consists only of a cleft in a mitral or tricuspid leaflet.
2. A frank defect in both septa is present.

Evolution of this classification was stimulated because of the clinical importance of distinguishing lesions not amenable to short open-exposure correction. The characteristic aspect of atrioventricularis communis is the presence of incompetence of one or both atrioventricular valves. This phenomenon results in a very different alteration in hemodynamics and thus a very different clinical entity than with atrial defect alone, where the valves are both competent. Thus, the hypertrophy of the left ventricle, the lack of marked right-sided preponderance in the electrocardiogram, and the presence of a blowing systolic murmur heard best at the apex or just to the left of the sternum in the fourth and fifth interspaces are distinctly at variance with the findings in defects of the atrial septum alone. Moreover, since the septal leaflets of both the mitral and tricuspid valves embryologically are derived from the tissue which also forms the ventricular septum, a congenital defect of these structures, it seems to us, should be considered as a variant of ventricular rather than atrial septal development. When associated with a hole in the atrial septum, such a combination is truly atrioventricularis communis, in its mildest form.

TABLE I. DISTRIBUTION OF ANATOMIC TYPES OF ATRIAL SEPTAL DEFECTS AND THEIR ASSOCIATION WITH ANOMALOUS PULMONARY VENOUS DRAINAGE

TYPE OF LESION	NUMBER	NUMBER WITH ANOMALOUS PULMONARY VEINS
Foramen Ovale Defects		
1. Defect in valve	77	2
2. Valve absent	9	4
Septum Secundum Defects	12	10
Combined Defects	2	0
Totals	100	16

With this classification, then, septum primum defects become extremely rare. Most lesions which others might classify in this fashion are associated with a mitral cleft and thus we classify them as a variant of atrioventricularis communis. On the basis of this classification, the distribution of cases in this series is presented in Table I.

CLINICAL MATERIAL

The first patient in this series was a 26-year-old woman who was operated on April 15, 1953; the one hundredth was an 8-year-old girl operated on Jan. 14, 1958. The age span was from 10 months to 45 years, distributed as shown in Fig. 1. The jump in incidence in the 6- to 10-year group may be a function of school entrance examinations at age 5 or 6. The large number of relatively old patients coming to surgery for a congenital defect reflects the lack of a previously available method of repair. A large backlog of untreated patients exists in the population. It is to be hoped and expected that as the years go by, with greater awareness of the desirability of early treatment on the part of physicians in general, most of the patients with this disease will be recognized at grade school age and referred for treatment when the operative risk is very low, in fact, roughly equivalent to that for repair of patent ductus arteriosus.

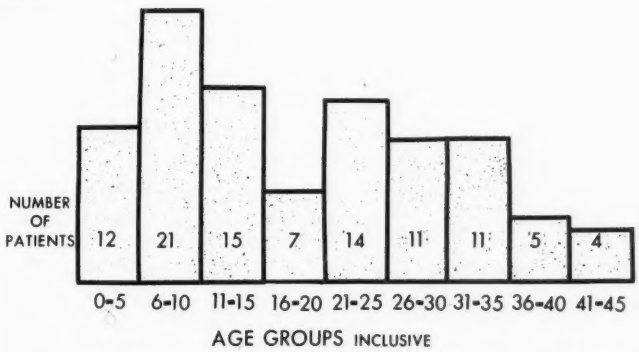


Fig. 1.—Age distribution at surgery for atrial septal defect (100 cases).

It is worth noting that the influence of sex on the incidence of this disease is quite pronounced. Our experience is similar to that reported by many others. We had 68 female patients, as compared to 32 males. Since roughly two out of three defects occurred in females, the sex of the patient becomes a minor factor in the diagnosis.

THE NATURAL HISTORY OF ATRIAL SEPTAL DEFECT

During fetal life, the presence of an atrial septal defect places no increased burden upon the circulation, as the normal blood flow passes from right atrium to left. Following birth, a left-to-right shunt at this level is prevented by the closure of the foramen ovale. However, if a considerable atrial

septal defect is present, the two ventricles fill from a common source, and what complement of blood each receives depends on the resistance to filling which each offers.

Thus, at birth, the heart size in such a situation is normal, and it is rare for a patient whose sole malformation is an atrial septal defect to die in the first year of life. At birth, moreover, the right and left ventricles are of about equal muscular development and the pressures in the systemic and pulmonary circuits are about equal. As time goes by, however, there is a fall in pulmonary vascular resistance and a rise in systemic resistance. Concomitantly, the muscular development of the left ventricle comes to exceed that of the right, and the resistance to ventricular filling likewise becomes greater on the left side. Thus, it is easy to understand the gradual increase in the left-to-right shunt through the atrial septal defect as the resistance to passage of blood into right ventricle and pulmonary circuit becomes significantly less than that into left ventricle and aorta. This change occurs relatively slowly during the first year of life and the circulation is able to adapt itself to the derangement of hemodynamic pattern. The right ventricle and pulmonary artery pressures fall, and the normal regression of the fetal pulmonary vascular pattern takes place.

Accordingly, the patient with an atrial septal defect usually does very well in the first year of life, and rarely is the diagnosis made at this time. A further factor that may operate in this period is that, as the right atrium dilates, the atrial septal defect probably increases in size, further augmenting the left-to-right flow. Thus, most patients with this lesion have little in the way of symptoms during the first decade, and often the second as well. Frequently, however, they begin to note the development of symptoms in the third decade of life, consisting of insidious fatigue and dyspnea on exertion. The progression of the average case from this point onward can, so it seems, proceed along two paths.

First, a large pulmonary blood flow may be maintained, with a large left-to-right shunt at the atrial level and a low pulmonary vascular resistance. What rise there is in pulmonary artery pressure is on the basis of a large flow. Extreme dilatation of the right heart occurs, tricuspid valve insufficiency supervenes, and congestive heart failure with its typical features and sequelae may ensue, even in the presence of greatly increased right ventricular stroke volume and pulmonary blood flow.

Second, and more commonly, the natural history of the anomaly is governed by the development of obliterative disease in the pulmonary vascular bed, due perhaps to autochthonous thrombosis or miliary embolization associated with reversible and later irreversible arterial changes.

With the rise of pulmonary artery pressure that accompanies these changes, there is increasing hypertrophy of the right ventricle and increasing resistance to emptying of the right atrium. The left-to-right shunt at the atrial level diminishes in magnitude and may become balanced or reversed. The right

ventricle eventually fails under the stress of the pressure load against which it must work—as against the more easily borne volume load of the patient whose pulmonary resistance remains low.

It must be emphasized that all combinations of these two types of process may be seen, and at all ages. The youngest patient in our series was operated on at the age of 10 months. We have seen patients in their seventh decade who still had a high pulmonary flow and a low resistance. We have seen patients under 10 years of age who had severe pulmonary vascular changes and a balanced or reversed shunt. Finally, we have seen patients pass in a few years from the first group to the second in a period as short as a year or two.

It is with a background of this knowledge of the pathology and natural history of the disease that each patient is assessed, and only thus can the indications for surgery be clearly formulated.

INDICATIONS FOR SURGERY AND SELECTION OF PATIENTS

Early in the experience of this center, when the surgical risk was higher and complete cure in doubt; and with the knowledge that the defect is relatively benign as compared with other congenital heart defects, there was a natural hesitancy in advising operation. However, this had changed. Our confidence has increased as it has become increasingly apparent that this is a low-risk operation—there has not been one operative death in the last 57 patients. Furthermore, postoperative catheterization data have shown that the procedure is curative, and observation of the patients after surgery reveals what benefits can come to them. While the outlook is on the whole relatively good for a patient with an atrial septal defect, it is nevertheless still true that the mean life expectancy is not much over 37 or 38 years. We know, too, that when trouble comes along, it may cause rapid deterioration, and we cannot predict exactly which patient will be thus affected. Therefore, at present, the diagnosis of the uncomplicated lesion in patients under 40 years of age is sufficient to be a firm indication for its surgical correction. Even in the very young age groups, surgery is strongly advised even though the patient is entirely asymptomatic. We believe that if an atrial septal defect is obliterated below the age of 8 years, the patient has an excellent chance of having a normal cardiovascular system by the time he grows into adulthood.

It is also considered that what risk is present is less in the younger age groups; we have had only one death below the age of 18 years in a patient with an uncomplicated defect.

The real decision, then, is when not to advise surgery, and this can, at times, be very difficult. The obvious patient to whom surgery must be denied is the one whose pulmonary resistance is so high that the interatrial shunt is balanced or reversed. The value of surgery lies in closing the defect and abolishing the increased pulmonary blood flow. In such a patient, surgery does not help and the operative risk is high. In general, it is true to say that with increasing pulmonary vascular resistance the benefits derived from surgery decrease while the risk of surgery increases commensurately. Where precisely the dividing line should be drawn is not easy to decide. However, in these cases

with a high pulmonary vascular resistance, a pulmonary blood flow of no more than one liter higher than the systemic should raise serious doubts as to the advisability of surgery.

Preoperative Assessment.—The diagnosis of an atrial septal defect is based upon careful clinical evaluation of the patient. Earlier in this unit's experience, the help provided by cardiac catheterization was also called upon to provide confirmation of the diagnosis, and to provide a series of values with which the postoperative results could be compared. Nowadays, it is believed that the diagnosis can be accurately established clinically in 90 per cent of cases, except in the evaluation of the presence or absence of anomalous pulmonary venous connections. However, these can be recognized and dealt with so expediently at surgery that this does not prove a serious practical problem.

The clinical assessment encompasses history, physical examination and consideration of the electrocardiographic and radiologic features. Much has been written about these, and therefore they will be mentioned only briefly, with details of the findings in this series. It must be stressed that, despite the broad limits imposed, this remains a group of patients selected for their surgical suitability.

History: The symptoms varied from none at all to marked incapacity. The most obvious were dyspnea and fatigue, these being present in like measure. Before surgery, 38 patients were essentially asymptomatic, 29 had mild, 23 moderate, and 10 severe disability.

Orthopnea was present before surgery in 5 cases.

Palpitation, expressed as such or as "pounding in the chest," was a not uncommon symptom, being experienced by 24 patients.

Chest pain was prominent in the histories of 10 patients, but only in 3 of these was it suggestive of coronary insufficiency.

A story compatible with congestive cardiac failure had been given in 7 cases.

Pulmonary infections had been prevalent in 31 of the 100 patients. Of these, 9 had had pneumonia in early life, while 7 had grown out of this predilection after the first few years.

Cyanosis on exertion was questioned in 6 cases on historical grounds.

Syncope, particularly on exertion, was prominent in the stories of 12 patients.

Physical examination: Most of the patients were underweight with respect to their height, and some (but by no means all) were undoubtedly of the asthenic or "gracile" habitus. A precordial bulging was present in 40 patients. The venous pressure was not usually elevated, although in the children with a very active heart, it was sometimes as high as 2 to 3 cm. above the sternal angle, a level we did not consider abnormal. A systolic thrill in the "pulmonary area" was observed in 7 cases. The precordium was always hyperdynamic in the region of the left lower sternal edge, and the lift of pulmonary artery expansion was usually felt. The shock of closure of the pulmonary valve was frequently appreciable. On auscultation, the classical systolic

murmur caused by the passage of large volumes of blood through the pulmonary valve was heard in every case, maximally in either the second or third left intercostal space. A short diastolic murmur, heard either at the left lower sternal edge or more toward the apical region, was audible in 51 cases. This was considered to be due to increased volume of flow through the tricuspid valve. In no case, in the final analysis, was the diagnosis of "Lutembacher's syndrome" (i.e., atrial septal defect plus mitral stenosis) seriously entertained, and in no case was it found.

In 10 patients, the presence of a high-pitched blowing systolic murmur was detected along the lower left sternal border, and was considered to reflect tricuspid insufficiency. The murmur of pulmonary insufficiency was heard in 5 cases.

The second sound at the base of the heart was, in all cases except those with a high pulmonary vascular resistance, widely split and fixed with respect to the respiratory cycle. In the exceptional case with pulmonary hypertension due to increased resistance, the split was narrow or single, and the pulmonary element of the second sound loud.

The electrocardiogram: In no case was this normal. The degree of departure from normality was related to the extent of right-sided hypertrophy, this being interpreted, according to the findings, as reflecting hypertrophy of the right ventricle itself (RVH), its outflow tract (RVOH), or the region of the crista supraventricularis (CRISTA), the latter being the mildest form of abnormality. Though to some extent undoubtedly arbitrary, this classification has been found useful in comparing pre- and postoperative findings, and in relating the changes to the hemodynamic and anatomic findings. This subject will be thoroughly discussed in a subsequent publication.

RVH was present before surgery in 53 cases, RVOH in 44, and CRISTA in 3. The electrocardiogram showed the classical "partial right bundle branch block" pattern in most cases, although when the right ventricular hypertrophy was severe a qR pattern appeared in the right precordial leads. Some of the patients revealed the pattern of so-called "complete right bundle branch block" but we have been able to see no particular virtue in fixing an arbitrary limit for the QRS duration which separates a partial from a complete block.

Fluoroscopy and x-ray: Fluoroscopy was of the greatest help in the diagnosis. The heart was invariably enlarged, this being due to increased size of the right atrium and ventricle. The pulmonary arteries were large and pulsatile, and the vascular markings of the lungs exaggerated. The over-all activity of the heart was seen to be increased, the exaggerated excursion of the cardiac border being due to the increased stroke-volume of the right ventricle. The left atrium, left ventricle, and aorta were never prominent in the patient with an uncomplicated defect. In the 2 patients with an additional patent ductus arteriosus, however, the aorta was thought to be more conspicuous than usual.

Cardiac catheterization: Cardiac catheterization was performed prior to surgery in 93 cases, mostly at this center but also at various others where evaluation had been carried out before referral here.

The ratio of pulmonary index: systemic index was greater than 2.0 in 83 of the catheterized patients, and between 1.5 and 2.0 in 10. The total pulmonary vascular resistance, expressed as dynes-sec.-cm.$^{-5}$/M.^{2} exceeded 800 in 3 cases, the values being 910, 1,080, and 1,530, respectively.

Slight arterial unsaturation, less than 92 per cent, was found in 26 patients, but all of these had appreciable left-to-right shunts at the atrial level, and the oxygen level usually reflected mixing of blood in the two atria rather than a right-to-left shunt due to hypertension of the lesser circuit.

Anomalous pulmonary venous connections were found at catheterization in 8 patients.

Summary of preoperative diagnosis: On the basis of the procedures outlined above, 100 patients were selected for surgery with the diagnosis of atrial septal defect, secundum variety. Two were considered to have in addition a patent ductus arteriosus, and 8 to have anomalous pulmonary venous connections in addition to the atrial septal defect. In no case was the diagnosis of Lutembacher's syndrome made, and in no case was an ostium primum or atrioventricularis communis lesion suspected. Moreover, in no patient not included in this series was a diagnosis of septum secundum defect made when a septum primum or atrioventricularis communis defect was actually found at surgery.

HYPOTHERMIA

The growth and development of the use of hypothermia in this clinic have been the subject of many communications. As we have matured in the management of this modality with increasing experience, we have stablized our technique to include several specific procedures and precautions. When used within these limitations, it is our opinion that circulatory occlusion during hypothermia per se is a procedure essentially without risk; that is to say, considerably less than 1 per cent. Since, in our hands, this is considerably safer than other open-heart techniques for short procedures, we have continued to use the method despite the ready availability of cardiopulmonary bypass.

These general precautions in the use of hypothermia may be summarized as follows.

1. The range of the lowest rectal temperature achieved is 30° to 32° C. Circulatory arrest is performed at this temperature. This limitation in degree of hypothermia is extremely important.

2. Cooling is accomplished simply by immersion in ice water. There appears to be some rationale in cooling the peripheral tissue ahead of the heart and other vital organs.

3. Throughout the entire procedure, a deliberate respiratory alkalosis is maintained by hyperventilation.

4. Throughout the course of the cooling, operation, and warming, dextrose is administered intravenously. Evidence is increasing that intravenous nutrients have a beneficial effect on the myocardium in hypothermia.[40]

5. The first two units of blood used during operation are heparinized, having been freshly drawn in plastic bags. The presence of platelets, fibrinogen,

and other enzyme elements of the clotting mechanism, together with the absence of citrate, are considered helpful in avoiding the bleeding diathesis of hypothermia. Transfusion is given freely because a low blood volume is poorly tolerated in hypothermia.[41]

6. A bilateral sternum-splitting incision is always used in order to achieve adequate exposure and allow proper positioning.

7. Great care is taken to position the patient so that the cardiotomy is in the uppermost portion of the heart, thus materially reducing the risk of air embolism occurring in the coronary arteries.

8. After the establishment of inflow occlusion to the heart the coronary circulation is perfused with 1 to 2 c.c. of 1:4,000 neostigmine in order to slow the heart. The decreased metabolic needs of the slowly beating heart apparently are important in reducing the risk of ventricular fibrillation.

9. The root of the aorta is always clamped to prevent coronary blood flow during occlusion. This helps avert coronary air embolism, maintains bradycardia, and diminishes the coronary return to the heart, thus ensuring a dry operative field.

10. The period of circulatory arrest must not exceed 6 minutes. If more time is needed to complete the procedure, the operation should be interrupted and the circulation restored. A second period of occlusion can then be instituted after an appropriate interval to complete the procedure. The principle of multiple short occlusions allows at least 10 minutes of safe intracardiac time.

11. Warming is achieved by diathermy, which is a form of internal warming. There appears to be some rationale for rewarming vital internal organs before peripheral tissues.

OPERATIVE TECHNIQUES

The chest is prepared for a bilateral, transsternal thoracotomy which is made in the fourth intercostal spaces, and which is carried across the sternum in a "V" fashion to permit a strong mortice closure. A rib spreader is introduced at the level of the sternum and gradually opened as the suspensory ligaments of the pericaridum are divided. Meticulous hemostasis is observed.

Visual and palpatory examination of the mediastinum and heart are conducted after the pericardium has been opened to confirm the preoperative diagnosis and to search for other attendant anomalies, such as: anomalous drainage of the veins of the right lung into the right atrium or superior vena cava, pulmonic stenosis, patent ductus arteriosus, and persistent, left superior vena cava. In the latter event, the hemiazygos vein may join the left superior vena cava just before the junction of the latter with the coronary sinus (Fig. 2, *d*). If steps are not taken to occlude both of these vessels during cardiotomy, an annoying amount of venous blood will continue to flow from the ostium of the coronary sinus and compromise the technical exposure.

Umbilical tapes are passed about the superior and inferior vena cava intrapericardially. To encircle the superior vena cava, the pericardial reflexion

which binds it to the underlying right pulmonary artery must be divided carefully. The tape about the inferior vena cava should be placed as caudad as possible so that it will not interfere with the repair of the defect if it is associated with a prominent valve of the inferior vena cava.

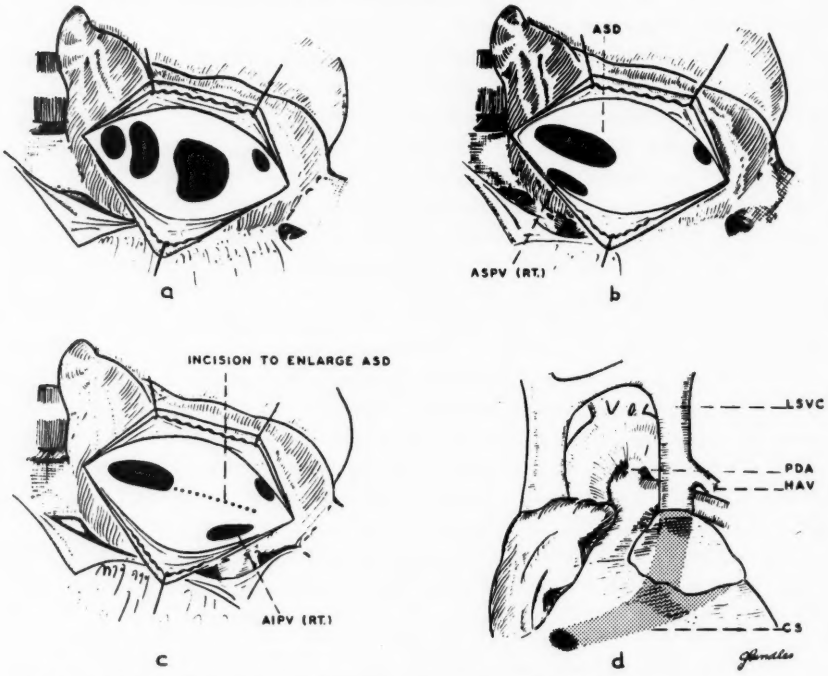


Fig. 2.—Some anatomic variations encountered in secundum defects.
a, Multiple openings involving both the foramen ovale and the septum secundum.
b, Septum secundum defect with anomalous right superior pulmonary vein.
c, Septum secundum defect with anomalous right inferior pulmonary vein.
d, Patent ductus arteriosus or left superior vena cava with hemiazygos vein may be present and should be carefully looked for before circulatory occlusion is attempted.

The wall of the right auricle is invaginated to permit palpation of the interatrial septum. In many patients we placed a purse-string suture on the right auricle tip and made a digital examination of the interior of the auricle. We found that our efficiency by this maneuver in describing precisely the pathology which was later seen through the open cardiotomy was only about 80 per cent. We missed some of the defects when they were multiple, some of the anomalous veins, and the relation of the inferior vena cava to the defect. Perhaps had we persisted we might have improved our sense of "feel," but since we found the procedure inaccurate and unnecessary we abandoned it.

Quadrant stay sutures of silk are now placed in the atrial wall overlying the defect to permit an atriotomy which will run diagonally from the inferior vena cava toward a point about midway between the superior vena cava and the right auricular tip. A noncrushing clamp is placed over the stay sutures and an atriotomy performed, about 5 cm. long. By tilting the patient to the

left, and with the head of the table well elevated, the plane of the interatrial septum is brought into a horizontal position, and the atrial septal defect is placed in a superior position relative to the left ventricle and auricle. This maneuver we consider very important in the prevention of coronary air embolism.

The ligatures about the venae cavae are tightened and about 30 seconds allowed for cardiac emptying to occur. The aorta is occluded distal to the coronary ostia and 1.0 to 2.0 c.c. of 1:4,000 neostigmine (depending upon the size of the heart) is injected into the aortic root. Coronary perfusion of this parasympathomimetic drug is achieved by the cardiac contractions. The aortic

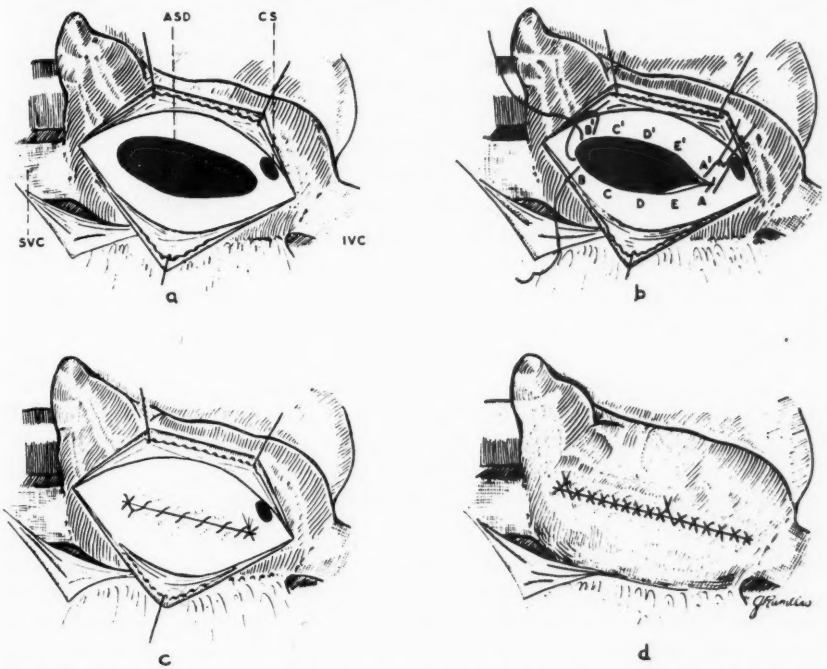


Fig. 3.—The surgical steps taken in the closure of a typical simple defect of the foramen ovale type.

a, The relationship between the atrial septal defect *(ASD)* and the coronary sinus *(CS)* is shown.

b, A mattress suture has been placed at the lower end of the defect. This is tied before a similar suture is placed at the upper end. The closure will approximate *A* to A^1, *B* to B^1, etc.

c, The upper suture has been used as a continuous stitch and then tied to one end of the first (lower) mattress suture.

d, The auricular wall is closed with continuous mattress sutures to enhance control of bleeding from the auricular wall arteries.

clamp is removed and a right angle or oblique nonerushing clamp is introduced through the transverse pericardial sinus to occlude aortic and pulmonary artery flow. This clamp is placed against the very base of the aorta snugly to occlude the coronary ostia and discourage coronary air embolization.

The atrial clamp is removed and the heart emptied by aspiration. Free of blood, the atria collapse, and the lips of the septal defect coapt. If the holes

are multiple, they are converted to a single opening by excision of the thin partitions (Fig. 2, *a*). The locations of the tricuspid valve, coronary sinus, inferior vena cava, superior vena cava, and orifices of the pulmonary veins are ascertained. A finger is placed into the mitral valve, transseptally, to assure its adequacy. A figure-of-eight suture of 2-0 silk is placed in the most caudad aspect of the defect and held by an assistant. The ligature about the inferior vena cava is loosened momentarily so that a free flow of blood from its orifice will establish its relationship to this first suture. A similar stitch is placed in the caphalad angle of the defect and run as a continuous suture caudad to be tied to the original suture. Prior to this final maneuver, the last few millimeters of the defect are permitted to gape while the right atrium is flooded with blood from the superior vena cava. In this way, residual air in the left atrium is allowed to escape as this chamber is filled with blood. The final tie is completed. The superior vena cava is released thus filling the right auricle. The atriotomy clamp is applied, and the clamp across the great vessels removed. The right coronary arteries are scrutinized for evidence of air emboli. (If emboli are noted, the aorta is clamped distal to the coronary ostia and manual, intermittent cardiac compression introduced immediately to propel the air distally.) Without such a complication, however, the vigor of the myocardial contraction slowly improves. The inferior vena cava tape is removed and cardiac action resumes its preocclusion characteristics. Interestingly, a transitory, systemic hypertension often occurs at this time.[42] Rewarming is begun.

The atriotomy is closed with a continuous mattress suture in order to occlude the atrial branches of the right coronary artery which, on two occasions before this suture was adopted, caused trouble by postoperative bleeding. Bilateral, posterior chest tubes are placed. The wound is closed in layers with steel wire sutures to the sternum and interrupted silk stitches to the muscular and fascial layers.

The total time of circulatory occlusion is now limited to 6 minutes; a period deemed safe on the basis of both laboratory and clinical experience. It has been impossible to close all of the defects in 6 minutes. In such circumstances, an additional period of occlusion has been used with intervening periods of normal flow lasting 10 to 20 minutes. Four patients have undergone multiple occlusion, all with good results.

One of the pitfalls in the repair of what appears to be a simple lesion is the failure to recognize the fact that the Eustachian valve of the inferior vena cava forms the lower margin of the defect. Closure of these enticing margins will transplant the vena cava to the left auricle, a fatal technical error. To reassure ourselves that the inferior vena cava is entering the right side of the inferior end of the suture line, we release for a moment the tape on this cava to observe directly the exact point of entry of this structure into the auricle. The maneuvers taken to correct this anomaly are illustrated in Fig. 4. Essentially, total excision of the valve itself is the primary maneuver. The lower stitch in the closure of the defect must now be placed high enough above the

mouth of the cavae to allow free entry into the right auricle. Significant partial obstruction of the inferior cava is probably not tolerated by man any more readily than it is by the experimental animal.[43]

If anomalous drainage of a right pulmonary vein is associated with persistence of inferior vena cava valve, the repair will involve enlargement of the auricular defect in accordance with general principles to be described below. A final measure to avoid any possibility of vena cava pressure is to clean the epicardium from the auricular muscle at the point of entry of the vessel. In one instance, we felt it desirable to perform what was essentially a "pyloroplasty" at this point to enlarge the mouth of the cava toward the right.

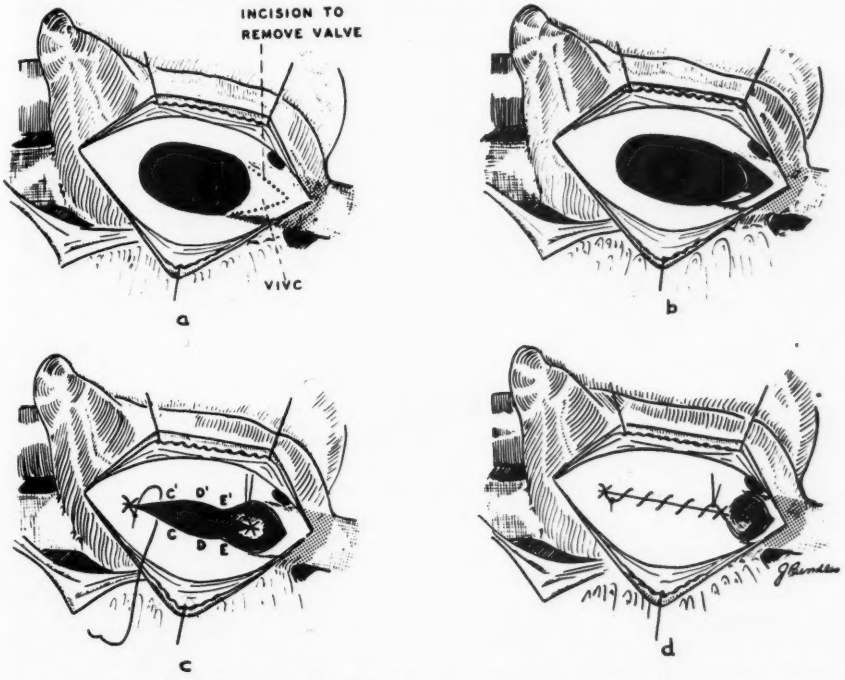


Fig. 4.—A false impression that the inferior border of the defect is the valve of the inferior vena cava *(IVC)* can be easily held. Simple suture of this apparent defect is fatal, since the inferior vena cava will enter the left auricle. The steps in the repair are illustrated.

a, The valve of the inferior vena cava *(IVC)* is excised along the dotted lines.

b, The true edges of the septal defect can now be seen.

c, The two mattress sutures have been carefully placed and the upper one is being run as a continuous stitch.

d, The completed closure leaves the inferior cava entering the right auricle.

As mentioned, 14 patients had anomalous pulmonary venous drainage from the right lung and one patient had anomalous return from the left via the coronary sinus. In every instance save one it was possible to devise an operative procedure which would redivert all the pulmonary blood into the left auricle and at the same time close the communication between the two auricles. In the remaining patient one small anomalous vein high on the vena cava remains untreated. This maneuver usually involves enlarging the atrial septal

defect so that an opening is created through which the anomalous veins may drain freely to the left side without any obstruction. The effect of pulmonary venous obstruction has been previously described.[44] Such obstruction is highly undesirable, since the pleural adhesions which will form and through which will flow the pulmonary venous blood constitute a right-to-left (lung to thoracic wall venous system) shunt that will defeat the purpose of the operation. Every precaution must be taken, therefore, to avoid pulmonary venous congestion in these maneuvers. It is for this same reason that simple ligation of a single anomalous pulmonary vein entering high on the vena cava will result in no beneficial effect whatsoever. In this rare circumstance, if the vein cannot be safely transplanted, simple ligation of the pulmonary artery to the pulmonary segment is the procedure of choice, while the vein is not

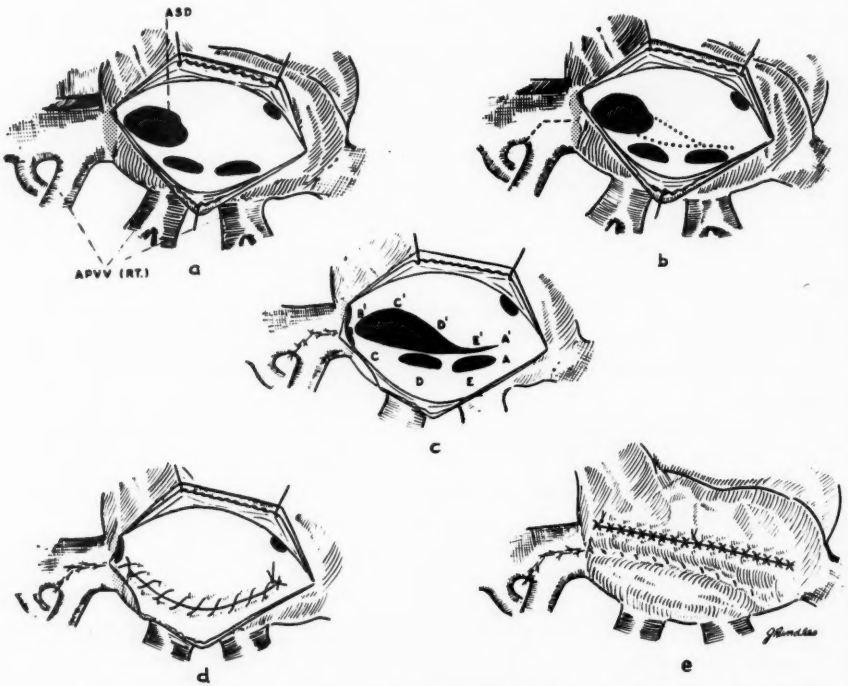


Fig. 5.—The surgical steps in the repair of a patient with defect of the septum secundum associated with total anomalous pulmonary venous drainage from the right lung are illustrated.

a, The most superior anomalous pulmonary vein enters the superior vena cava; two other right pulmonary veins enter the right auricle.

b, The first steps in the repair are shown. An interrupted suture line will be placed in the superior vena cava as indicated by the broken line, thus bringing pulmonary vein blood into the right auricle through a separate lumen which will be made to enter left auricle when the septal defect is closed. This defect must first be enlarged, however, by incisions along the dotted lines.

c, After placing the vena caval sutures from outside, the septum is opened and the proposed closure is indicated by the letters *A*—*A*^{1}, *B*—*B*^{1}, etc.

d, The completed suture line is shown. The lateral bites of each stitch are taken well up on the lateral wall of the right atrium, thus protecting against pulmonary venous congestion by enlarging the left auricle.

e, The completed operation is shown following auricular wall closure. The amount of right auricular wall used to enlarge left auricle is seen in the lower portion of the diagram.

molested. Thus, bronchial artery blood will nourish the lung and drain to the cava. If the operator desires to indulge in segmental resection, it will be curative but the risk will be greater.

When the highest pulmonary vein or veins enter the superior vena cava just above the right auricle and below the azygos vein, as is commonly the case, the maneuvers illustrated in Fig. 5 have proved satisfactory. The first critical consideration is the separation of the systemic from pulmonary venous flow within the vena cava by converting that structure into a double-barreled vessel. The pulmonary limb is made definitely adequate *even at the expense of what the operator would desire for the caval blood.* The azygos vein is carefully preserved in this procedure to provide a safety valve, and we have seen

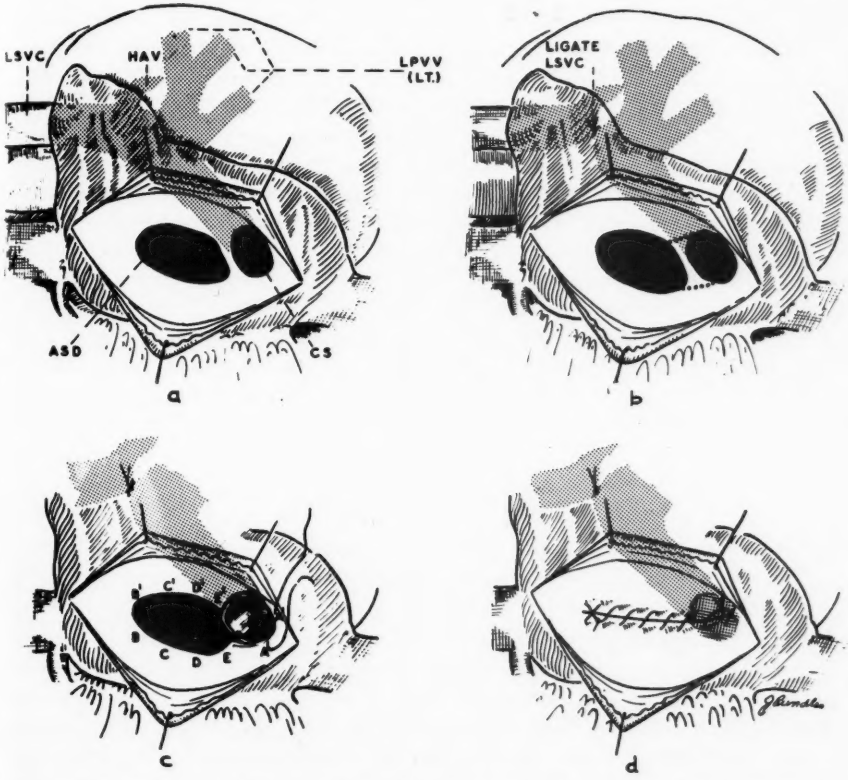


Fig. 6.—The steps taken to solve the problem of total left anomalous pulmonary venous drainage via the coronary sinus are illustrated.

a, The pertinent anatomy of the defects is diagrammatically presented. Note the persistent left superior vena cava *(LSVC)*, hemiazygos vein *(HAV)*, and the drainage of the left pulmonary veins *(LPVV)* into the coronary sinus.

b, The left superior vena cava has been ligated below the hemiazygos vein. The tissue separating the defect and the coronary sinus, together with the wall of the coronary sinus as it traverses the left auricle, will be excised.

c, The coronary sinus will now be transplanted to the left of the closure when *A* is approximated to A^1, *B* to B^1, etc.

d, The closure has been completed. The entire pulmonary venous drainage now enters the left auricle as does the blood from the coronary sinus.

no difficulty result from this procedure in these patients. This entire maneuver can be readily done from without, i.e., a closed maneuver, before the auricle is opened, by a row of mattress sutures placed along the side of a Potts clamp or even without such a clamp being used. The sutures are passed from in front of vena cava to the back and then redirected anteriorly, where they are tied.

The second consideration is the enlargement of the atrial septal defect so that the veins and the new limb of the superior vena cava may be transposed.

The final consideration is the deliberate use of a centimeter or more of right atrial wall to add to the left atrium. By coming anteriorly in this fashion and using some of the abundant right atrium, any tendency to squeeze the pulmonary veins by the septal closure is avoided. In effect, this maneuver moves the posterior attachment of the atrial septum to the right and anterior, thus enlarging the left atrium which is, of course, hemodynamically desirable.

One final, albeit rare, anatomical variant is illustrated in Fig. 6. The left pulmonary veins entered a left superior vena cava which drained into right auricle via the large coronary sinus. By enlarging the septal defect and excising the upper lip of the coronary sinus (Fig. 6), a single defect was created which could be readily closed by continuous suture. The flow through the coronary sinus now entered the left auricle. Following ligation of the left superior vena cava below the hemiazygos vein, this flow consisted of the entire venous drainage from the left lung and the coronary venous blood usually found in the coronary sinus. This small right-to-left shunt, however, is undetectable clinically, and the patient's course has been excellent. This patient's problem has been the subject of a separate report.[45]

REOPERATIONS

Four patients in this series were operated upon as second attempts to repair their defect. Three of these were patients on whom our original closed "button" techniques had been performed, but who were shown to harbor residual shunts. One of these (R.B.) was operated upon on June 4, 1952. The defect was partially closed, as we found at second operation, but hemodynamically, the shunt was still immense. The second was a young girl (D.D.) who had previously had a polyethylene button of considerable size fixed in position across the upper portion of her defect. She was much improved, but because of a large measured residual shunt, reoperation was performed. The button was found to be in excellent position occluding about 80 per cent of the defect. A crescent-shaped hole at the lower pole, however, remained. The button was left in place and the residual defect was closed by a series of sutures from rim to button. The third patient (W.G.) was similar to the second, and secondary repair was also successful.

The final patient (J.U.) was one in whom open operation had been performed. At the first procedure, he had a low lying defect, but one not technically difficult to close. Interrupted sutures were used. Recatheterization revealed him to be improved but not cured. A moderate shunt remained.

Accordingly, he was reoperated upon, and a slit-like opening not over a centimeter long was seen between two of the previously placed sutures. This was easily closed, and he has done well. As a result of this experience, we shifted to using a continuous suture to close the defect.

Our conclusions from this experience, therefore, may be summarized as follows. (1) Second bilateral thoracotomies during hypothermia are extremely difficult, and, we think, hazardous. The many adhesions which tend to bleed profusely add technical difficulties and require extensive transfusion. The time to cure a patient of atrial septal defect is at the first operation. (2) Only one goal for the operation is acceptable; namely, one hundred per cent closure of the defect. Eighty or ninety per cent closure is inadequate, since significant shunts will remain. (3) The desirability of open techniques where all defects can be seen and all anomalous veins transposed seems to us so obvious as no longer to need reiteration.

POSTOPERATIVE MANAGEMENT

Little is required in the postoperative care of these patients that is not observed following any thoracotomy. Blood loss from the chest tubes is replaced in equal volume. Narcotics are not administered until the patient is fully awake and his vital signs stable. Thereafter, narcotics or sedatives are given regularly every 3 to 4 hours, during the first day or 2 to diminish "splinting" of the chest due to pain. Venous pressure is assessed several times during the early postoperative period by direct measurement and also by observation of liver size and the height of jugular filling. Chest tubes are usually removed 24 hours after operation and ambulation begun. Myocardial failure is treated if and when it occurs. Prophylactic digitalization is not employed.

Adults with evidence of a large pulmonary vascular bed are placed on anticoagulant therapy as soon as the chest tubes are removed. Heparin followed by Coumadin is employed. The therapy, designed to prevent intravascular pulmonary thrombosis, is maintained for 2 to 4 weeks, or longer if indicated.

Bleeding tendencies, when they occur, are usually due to elevated titers of fibrinolysin, and are usually self-limited. Specific therapy consists of administering fibrinogen alone or in company with fresh, whole, warm, citrated blood. For maximal benefit, fibrinogen should be given rather rapidly in order to saturate the fibrinolysin enzyme system. Calcium chloride, Premarin, Adrenosem, and protamine sulfate have been used at various times empirically.

Occasionally, diathermy burns occur, despite attempts to avoid them by placing felt pads between the diathermy coils and the patient, foam rubber pads under the hips, and by keeping the diathermy leads from touching towel clips, electrocardiogram leads, and thermocouple wires. The diathermy is used intermittently. Two minutes on, alternating with one minute off, is the safest effective technique we have found.

COMPLICATIONS AND MORTALITY

Certain of the operative and postoperative complications encountered in this group were of a type common to any major thoracic operative procedure.

Others, however, were peculiar to the open-heart closure of congenital cardiac defects during hypothermia and, as such, stimulated our interest particularly. In this latter category may be included: ventricular fibrillation, coronary air embolization, bleeding dyscrasias, pulmonary vascular thrombosis, myocardial failure, peripheral neuropathy, and diathermy burns.

Ventricular fibrillation developed during the operative procedure 16 times in 12 patients. Of these, 11 patients were successfully defibrillated and are still living. The first patient to experience fibrillation was a young girl, early in our series, who was cooled to 23.2° C. Her ventricles fibrillated as she was transferred from the cooling tub to the operating table (mechanical trauma). Defibrillation was achieved with potassium chloride and the septal repair completed uneventfully. The remaining 11 hearts were defibrillated with electric shock, observing principles outlined previously.[46] Nine episodes of fibrillation occurred relatively spontaneously: one at the conclusion of cooling; one upon atriotomy; one upon closure of the septal defect; one during auricular closure; three upon resumption of circulation; and one each at 3 minutes and 4 minutes after resumption of circulation. No evidence of coronary air embolization was observed in any of these. Seven episodes developed in conjunction with some specific event. One during pre-occlusion manipulation, one during atrial closure in which the atrial clamp was seen to encroach upon the right coronary artery, one following the removal of padding from beneath the patient allowing the patient to fall to the table with a jar, and four were associated with air embolization of the right coronary artery. Almost all of the spontaneous fibrillations occurred when the body temperature was below 29° C. Since we have been using the range of 30 to 32° C., fibrillation has occurred only when coronary circulation has been obstructed by air embolization.

It has been our policy to place cylindrical pads in a "T" arrangement under each patient—the vertical pad under the right side of the horizontal pad which is in the mid-thoracic area. These serve to accentuate extension and to elevate the right shoulder and chest, thus aiding the exposure of the right auricle. During removal of these pads to facilitate thoracic closure, one of our patients dropped the intervening 2 or 3 inches to the operating table. This jolt served as sufficient stimulus to incite fibrillation. Electrical defibrillation was eventually achieved; but the resuscitation was arduous and the patient died suddenly 14 hours postoperatively, possibly from a terminal episode of ventricular fibrillation. Since this experience we have exercised utmost caution to protect the whole patient from any mechanical shock.

Air embolization of the right coronary artery was observed immediately after re-establishment of the circulation in 10 patients. In 4, this was followed by ventricular fibrillation, and in 6 no arrhythmia occurred. The uncomplicated outcome of these last 6 is due, we believe, to immediate vigorous steps taken to drive the air distally in the coronary circuit, i.e., cross-clamping of the ascending aorta distal to the coronary ostia, accompanied by firm, intermittent manual compression of the cardiac ventricles. The prevention of this complication depends on extremely careful attention to allowing all the air in the left

heart to escape before the final stitch in the septal defect is tightened. In complicated lesions, when time is running short, this maneuver may be performed too hurriedly to be effective.

Bleeding of marked degree occurred postoperatively in 6 patients in whom its cause was not readily explained, i.e., unrelated to bleeding from a specific vessel, or to anticoagulant therapy. Of these, 2 died of the hemorrhage. The operative temperatures ranged from 26.5° to 30.0° C. in this small group. The role played by temperature itself in the "bleeding diathesis" is uncertain, but since we have limited the temperatures to the range 30.0° to 33.0° C., bleeding has been no particular problem and has been associated with no fatalities. Our general approach to the treatment of this problem was outlined earlier.

As mentioned previously, we consider the possibility of pulmonary vascular thromboses a constant hazard in all adult patients with large left-to-right shunts. Our reasoning is that such individuals have a pulmonary vascular system of greatly expanded volume. This capacity remains more or less constant following closure of the defect, and, since the volume of pulmonary blood flow is much reduced, its velocity is correspondingly reduced. This relative stasis is conducive to thromboses in these vessels as elsewhere. Currently, all such patients are placed on anticoagulant therapy as soon as the chest tubes are removed. Prior to the inauguration of this plan, six instances occurred in which pulmonary thrombosis was strongly suspected; 3 of these patients died. The radiographic picture accompanying these changes is one of diffuse or scattered, progressive "bronchopneumonia" or "pulmonary infarction," and matches the pathologic changes previously demonstrated in the experimental animal.[44]

Fatal thromboses in other vessels developed in 2 additional patients, neither of whom was under anticoagulation therapy. A 6-year-old girl died 48 hours postoperatively of bilateral internal jugular vein thromboses. It was thought that tight adhesive tape encircling the neck to hold in the endotracheal tube may have been an etiological factor in this patient. A 21-year-old female developed an occlusion of the left carotid artery on the third postoperative day and died on the sixth. A 13-year-old girl experienced an embolus to her aortic bifurcation on the fifth postoperative day which was successfully removed. These episodes raise the question of whether or not an excessive state of hypercoagulability occurs postoperatively in these patients. That this may be so is strongly suggested by the studies of von Kaulla and Swan.[47]

Myocardial failure was noted in 9 patients postoperatively all of whom responded well to digitalis therapy. All of these patients were over 10 years of age, and 5 of them were over 25 years.

Two other complications are related to our method of inducing and relieving hypothermia. Four patients experienced a transient neuropathy of the hands or arms. This was found by Stephens and Appleby[48] to be a direct injury of the nerves due to cold immersion. Careful attention to preventing prolonged immersion of the extremities in the ice water has prevented subsequent similar difficulties. Diathermy burns occurred in 8 patients. Four burns, in adults, were sacral. Prevention is attempted by placing felt padding between the patient and the diathermy coil and foam rubber under the pelvis. Four

other patients were burned on the extremities where electrocardiogram electrodes or intravenous needles came in contact with the diathermy cables. Prophylaxis in this regard is obvious, and has been largely successful.

In this series, 93 patients survived their surgery. All 7 deaths occurred in the first 43 operations; the last 57 have been performed without mortality. Analysis of the causes of the deaths in the first part of the series led to the adoption of precautions which may be playing a role in the apparent improvement in operative risk. These deaths were primarily caused by the following factors:

Ventricular fibrillation	1
Blood clotting disturbance	
a. Bleeding	2
b. Postoperative thrombosis	4

Many of the precautions currently practiced to avoid these lethal complications have been already mentioned, but for the sake of emphasis we repeat them here. Ventricular fibrillation is minimized by:

a. Temperature not below 30° C.
b. Continuous respiratory alkalosis.
c. Constant intravenous glucose infusion.
d. Neostigmine by coronary perfusion at the start of circulatory arrest.
e. Careful avoidance of trapping air in left heart.
f. Avoid clamping right coronary artery in nonerushing auricular clamp.
g. Avoid jarring the cold patient.
h. Selection of patients who do not have nonreversible pulmonary hypertension (resistance over 700 dynes).

Disturbances in clotting mechanism are minimized by:

a. Temperature not under 30° C.
b. Preoperative treatment of a depressed prothrombin time with vitamin K[1].
c. The use of fresh blood in siliconized bottles for the first two units used at surgery.
d. Avoidance of constrictions of the neck during anesthesia.
e. Careful endocardium-to-endocardium closure of the auricle.
f. Postoperative anticoagulation of all adult patients with very large pulmonary vascular beds.

RESULTS OF SURGERY

Of the 100 patients in the series, 92 are alive. Seven died as a result of surgery, and one patient, aged 39, died 8 weeks after surgery from a cerebellar hemorrhage. It does not appear that this latter event can be related to the surgery; the patient was under the management of her personal physician and was taking anticoagulants at the time.

Of the 92 patients, we have recent information on 91. One lady we have been unable to trace, but learn that some months ago she removed to California. Forty-nine have been seen recently at this center; all the others live at considerable distances from Denver, and we have relied on the combined reports from the patients, their parents, and their doctors (frequently accompanied by roentgenograms and cardiograms) for an accurate assessment of their condition.

The follow-up is 5 years in 3 cases, 4 years in 7, 3 years in 17, 2 years in 21, one year in 31, and 6 months in 13 cases, respectively. We have therefore been able to observe the changes in symptoms, signs, electrocardiogram, and x-ray studies which come about as a result of closure of the defect.

SYMPTOMS

In order to gain an over-all picture of what change takes place, we must not forget that the disease expresses itself not only in terms of the major symptoms such as dyspnea, fatigue, and effort intolerance, but obtrudes into every small background pattern that goes to compose a patient's life. We have heard patients express their improvement in the fact of waking up refreshed instead of tired from a night's sleep, of being able to enjoy a late show or a late meal, of being able to go into the mountains without fainting, and so on. However, for the purposes of comparison, we shall confine ourselves to the major and overt symptoms which are more directly an expression of cardiovascular dysfunction.

For the purposes of analysis, we have again separated the symptoms into three grades: mild (Grade I), moderate (Grade II), severe (Grade III), stipulating broadly the criteria by which we put any given patient into a particular group.

Dyspnea and Fatigue.—

Of the 10 patients who suffered severe (Grade III) disability prior to surgery, 6 are now asymptomatic, while 3 were surgical mortalities. Of the 23 cases moderately incapacitated (Grade II) before surgery, 15 are now without symptoms while 2 are dead. Of the remaining 6, 3 are improved. Of the mildly (Grade I) incapacitated group of 29 patients, 27 are symptom free, one has as much disability as before, while one died at operation.

Thirty-eight patients were free from symptoms before surgery. Thirty-seven are now well, while one died following operation. Thus, of the 100 patients who went to surgery, 85 are now leading normal lives without significant symptoms.

TABLE II. EFFECT OF SURGERY ON THE SYMPTOMATOLOGY ASSOCIATED WITH ATRIAL SEPTAL DEFECT

SEVERITY	PREOPERATIVE STATUS	POSTOPERATIVE STATUS				DEAD
		0	I	II	III	
0	38	37	—	—	—	1
I	29	27	1	—	—	1
II	23	15	3	3	—	2
III	10	6	—	—	—	4
Totals	100	85	4	3	0	8

The rate at which improvement takes place after surgery varies from patient to patient. Naturally, in a series as large as this, many different types of reaction to the new-found health have been seen. A few patients have substituted "functional" symptoms for their previous organically engendered ones. Some improve rapidly after surgery; for example, one jockey, age 32, was racing again 3 weeks after surgery; another patient was seen by her proud medical attendants to climb to the top row of a football stadium without any

difficulty within 2 weeks of surgery. Most patients are leading normal lives within 2 or 3 months of operation, although in some cases slow improvement continues for upward of 12 months. There is usually a gain in appetite, weight, and zest for life; and many patients who had no real complaints before surgery state that they have gained in strength and energy, and only in retrospect do they realize that they were limited before.

The "Postcardiac Surgery" Syndrome.—

Previously described as the "post-commissurotomy syndrome" or "post-valvotomy syndrome," this illness has appeared since operation in at least 15 patients in this series. In a further 6, it may have occurred in a mild form. It differs in no way from the "post-commissurotomy syndrome" which follows surgery of the mitral valve, and is characterized by fever, malaise, pleurisy, and pericarditis. It responds rapidly to the administration of steroids, and untreated lasts from 7 to 10 days before subsiding spontaneously. In one patient, it has recurred 5 times, although most of the patients have had only one attack. In 2 cases, the illness appeared 8 days after surgery; in one not until a year later. When adequately treated it is not a significant cause of disability.

Changes in Physical Signs.—

As soon as the immediate postoperative period is past, it becomes possible to assess what changes had occurred in the physical signs. First, with the reduction in the stroke-volume of the right ventricle, the whole precordium became quieter and its activity less. In every patient, the systolic thrill disappeared. Almost invariably, the systolic murmur in the "pulmonary area" was less loud; in a few cases it disappeared completely. The residual systolic murmur was probably due to the persistent relative narrowing of the pulmonary valve in relation to the marked dilatation of the pulmonary artery causing turbulence and eddies. Gradually, over the ensuing months, the systolic murmur diminishes in intensity. The preoperative diastolic murmurs which are due to increased flow disappear. The rare diastolic murmur due to pulmonary insufficiency persisted in 2 cases and disappeared in 3.

The characteristic wide and fixed splitting of the second heart sound at the base has persisted unchanged in a few cases, but more commonly the sounds appear to return to a normal pattern with respiratory variation in the degree of splitting.

In summary, then, the changes which follow surgery consist of a diminution of precordial activity, disappearance of the systolic thrill, abolition or lessening of murmurs and, in most cases, a return toward normal second cardiac sound. This is, of course, usually accompanied by a diminution in heart size, and a gain in general physical well-being.

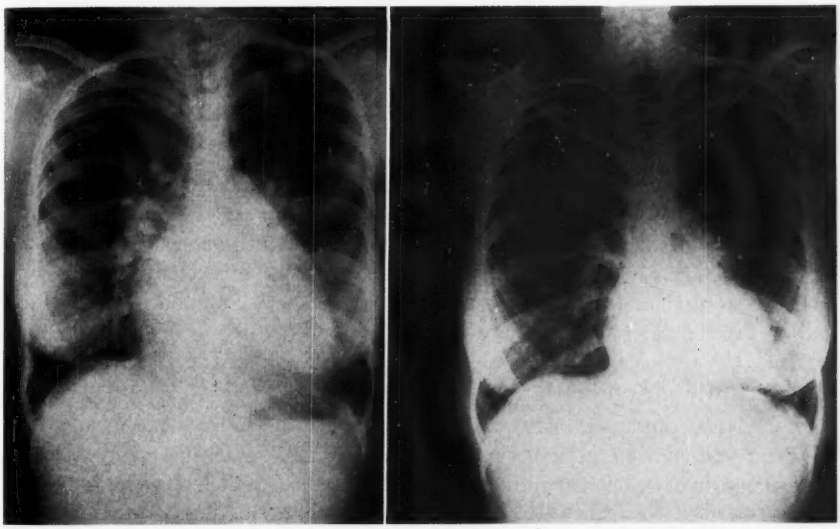
The electrocardiogram: We have had an opportunity to examine a recent electrocardiogram in almost all cases. When the defect has been closed, the tracing changes toward normal, the most characteristic feature being the diminution in the height of R′ (the secondary R wave) in the right precordial chest leads. In no case has this failed to occur except when the defect has not been

obliterated (2 patients), or when irreversible pulmonary hypertension is present (one patient). If this change is not manifest within about 4 months, it is meet to look for the reason.

The subject of postoperative electrocardiographic changes will be fully considered elsewhere.

Fluoroscopy: At the first postoperative fluoroscopic examination, the previously hyperdynamic heart is seen to have become quiet, and the excursion of the cardiac border much less. The characteristic cardiac contour remains, however, and the pulmonary artery is still prominent, though far less actively pulsatile than before.

As time passes, there is usually a real diminution in cardiac size in the individuals whose heart was significantly enlarged preoperatively (Fig. 7). The bronchovascular markings in the lung fields also become less apparent as time passes. Again, therefore, there is a gradual continuing regression toward normal, although, in the case of the adults in whom significant cardiac enlargement was present before surgery, it is doubtful if the heart size and contour will ever return completely to normal.



A. *B.*

Fig. 7.—The regression in the pulmonary vascularity and in the size of the heart, which occurred in the 2½ years after surgery in this 23-year-old girl, is evident by comparing the preoperative *(A)* and postoperative *(B)* films.

Cardiac catheterization: This was performed after surgery in 44 cases. In 39 of these the results showed that the left-to-right shunt had been abolished. There were 5 cases in which there was evidence of a residual shunt at the atrial level. In 2 of these cases this is of significance; a boy of 12 who was operated on in 1954 using interrupted sutures, and a lady of 45, operated on in 1957, who had an extremely large heart and huge defect. In the other 3 cases, normal postoperative improvement has occurred, both objectively and subjectively.

The results of postoperative catheterization showed clearly that the preoperative elevation of pulmonary artery pressure was in many cases due to the high flow, and that as soon as this was reduced the pressure fell. Of the patients with a very high pulmonary vascular resistance (800 dynes-sec.-cm.$^{-5}$ /M.^{2}) only one survived. She has recently been recatheterized, and the results show that there has been no regression in the severe pulmonary hypertension. Thus, on the basis of the objective evidence obtained by postoperative catheterization of almost half of these patients, the operation has been proved to be curative in the great majority.

SUMMARY

1. One hundred consecutive cases of atrial septal defect secundum seen at open-heart surgery have been analyzed and the data presented.

2. There were 7 operative deaths among the first 43 patients, none among the last 57.

3. The natural history of the disease, diagnostic criteria, and indications for surgery are discussed. It is urged that in the light of the safety of the operative procedure described, all patients with this diagnosis should be given the benefit of surgical repair unless the pulmonary resistance is greatly elevated.

4. The operative techniques employed to meet the various anatomic variations encountered are described. It is felt that hypothermia at the present time is the method of choice for the performance of these procedures.

5. The current status of all but one of the surviving patients is known and the data are analyzed. Eighty-one patients are symptom free and apparently cured by all means of assessment; 3 are improved but still have some symptoms; 3 have small residual shunts which do not seem to be of hemodynamic significance; one patient has become centrally cyanosed owing to the passage of inferior vena caval blood into the left atrium; one patient has persistent pulmonary hypertension after closure of the defect; 2 patients have residual shunts of sufficient degree to warrant re-intervention.

6. Atrial septal defect secundum is a congenital malformation which can be diagnosed clinically with great accuracy and which can be successfully treated surgically by open operation during hypothermia at a very low risk. Operation should be performed on essentially all patients with this disease during childhood, as soon as convenient after the diagnosis is made.

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THE ANATOMY OF ESOPHAGEAL HIATUS OF THE DIAPHRAGM AND THE PATHOGENESIS OF HIATUS HERNIATION

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DIAPHRAGMATIC hernias are not uncommon. From January, 1952, to January, 1957, our unit dealt with 142 cases of which 119 (80 per cent) were hiatus hernias (Table I). An investigation has been undertaken to determine the reasons for the susceptibilty of the esophageal hiatus to herniation. The results of the anatomic studies are described here; they largely confirm the findings of Allison,[1] and of Collis, Kelly, and Wiley.[5]

Thirty adult diaphragms have been dissected. Fifteen specimens were removed from fresh cadavers after the crural origins had been displayed and were then fixed to a wooden board and preserved in 10 per cent formalin. Fifteen were dissected in situ on embalmed bodies in the anatomy hall.

TABLE I. LIST OF CASES OF DIAPHRAGMATIC HERNA TREATED IN ONE UNIT OF THE DEPARTMENT OF THORACIC SURGERY, JOHANNESBURG AND BARAGWANATH HOSPITALS OVER A 5-YEAR PERIOD*

A.	*Traumatic Diaphragmatic Hernia*		12
	*Following penetrating wounds	4	
	Following crush injuries	5	
	Following operative trauma	3	
B.	*Congenital Diaphragmatic Hernia*		18
	Persistent pleuroperitoneal hiatus (Bochdalek)	3	
	Congenital absence of posterolateral part of diaphragm	3	
	Total absence left diaphragm	1	
	Congenital eventration of diaphragm	2	
	Parasternal hernia (Morgagni)	2	
	Aorta-esophageal hernia	1	
	Infantile hiatus hernia	6	
C.	*Acquired Hiatus Hernia*		112
	Adult type (sliding and rolling)	110	
	Acquired short esophagus (caustic stricture scleroderma)	2	

*Excluding acute penetrating thoraco-abdominal wounds.

THE CRURA

In 1907, Low published his classical account of the anatomy of the diaphragmatic crura. He considered that the esophageal hiatus was "formed by

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Received for publication April 8, 1958.

a splitting of the fibres of the right crus." This is an oversimplified description, as Collis, Kelly, and Wiley have shown.

The crura arise from one or more tendons whose fibers blend strongly with the anterior longitudinal ligament over the upper lumbar vertebrae. The left crus is usually attached to two lumbar vertebrae and the right to three, but they may arise at the same level from a common tendinous origin. Accessory tendons may arise from the fascia over the psoas muscles and from the medial arcuate ligaments but, though they form part of the crura, the fibers from these slips eventually fan out laterally to insert into the central tendon away from the hiatal limbs. The crura pass upward in close contact with the vertebral bodies for most of their course and only incline forward as they arch in front of the esophagus.

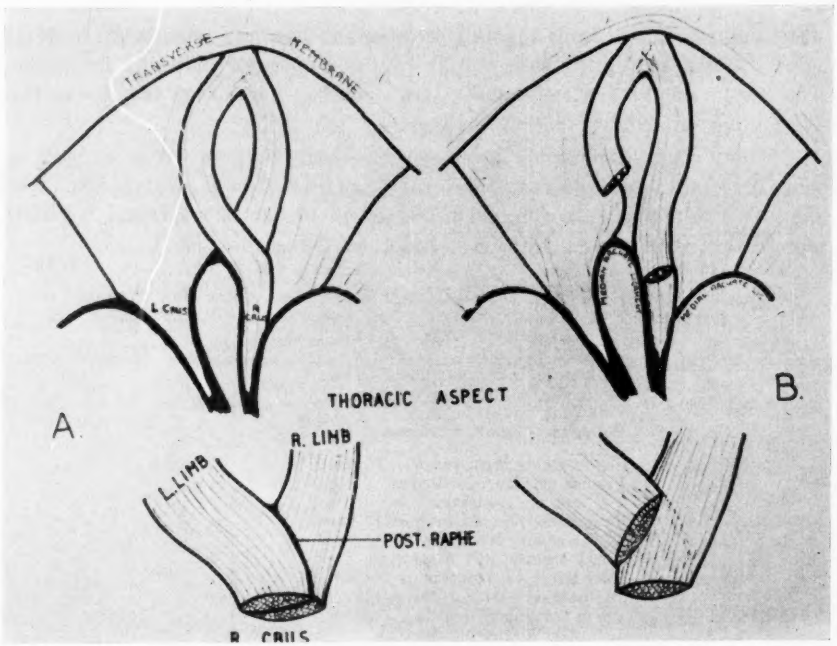

Fig. 1.—Illustration of the mode of formation of the hiatus. Two flattened muscle bands appear within the right crus separated by a plane of areolar tissue. The dorsal band forms the left hiatal muscle and the ventral forms the right hiatal muscle.

A, Muscle bundles intact. *B*, Segment of left (dorsal) limb of right crus removed to display the course of the right (abdominal) limb of the right crus. (*From* Marchand: Thorax 12: 189-202, 1957.)

As soon as muscle fibers appear within the right crus, they group themselves into two ribbonlike bands separated from each other by loose connective tissue. One bundle is dorsally placed (thoracic aspect) and the other ventrally placed (abdominal aspect). The dorsal band forms the left limb of the right crus and the ventral the right limb of the right crus (Fig. 1). The muscle bands soon diverge and cross each other in a scissorlike fashion, the ventral bundle passing

upward and to the right, and the dorsal bundle passing upward and to the left. The laterally placed fibers of each hiatal limb insert directly into the central tendon of the diaphragm but the medial fibers, which form the hiatal margins, incline toward the midline in front of the esophagus and decussate in a trellis-like fashion with fibers of the opposite limb (Fig. 2). Although there are many variations of this standard pattern, all embrace the basic principle of early grouping of flattened muscle bundles which diverge in a scissorlike fashion.

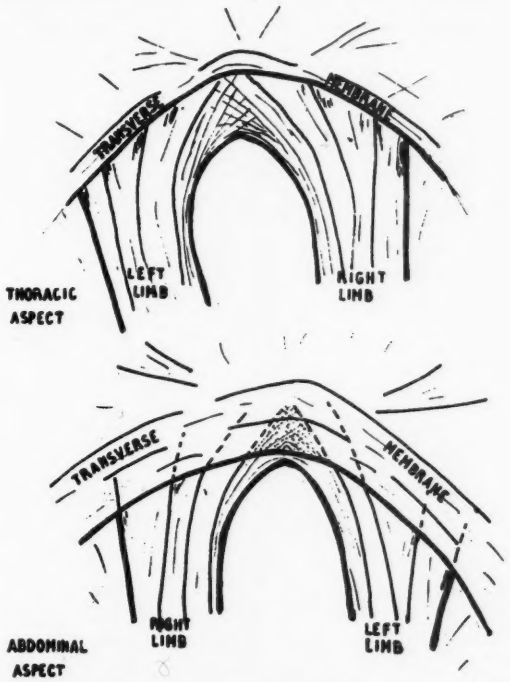

Fig. 2.—Diagram of the anterior edge of the hiatus illustrating the mode of insertion of the muscle fibers into the central tendon of the diaphragm. The medial fibers within each hiatal limb interlace with each other across the midline before inserting into the central tendon of the diaphragm. The transverse membrane of the central tendon supports the anterior decussating muscle fibers from the abdominal side. (*From* Marchand: Thorax, 12: 189-202, 1957.)

The Hiatal Orifice.—The hiatal orifice is elliptical in shape and its long axis lies in the sagittal plane. Sweet[20] and Harrington[9] have stated that the long axis lies transversely, but I agree with Allison[2] and Lam and Kenney[10] that this is not found in the normal body.

The elliptical shape arises naturally from the mode of origin and insertion of the hiatal muscles and the direction of their fibers. Any tendency toward widening of the transverse diameter is opposed by the crossover of the crural limbs and by the anterior decussating muscle fibers (Fig. 3).

Normally, about a centimeter of muscle separates the anterior rim of the hiatus from the central tendon of the diaphragm (Fig. 4). Lam and Kenney

state that the anterior margin of the hiatus is formed by the unyielding tendinous tissue of the middle leaflet of the central tendon, but this I have seen only when a hiatus hernia is present. On the abdominal aspect, a band of transverse tendinous fibers underlies the anterior decussating muscles and this may verge on the hiatal orifice. This transverse ligament is a strong fibrous band which reinforces the posterior edge of the central tendon of the diaphragm. It is about a centimeter in width and is best developed on the undersurface of the diaphragm where it forms a sharp falciform rim to the anterior edge of the hiatus. Here it supports the decussating anterior muscle fibers and resists any force exerted from the direction of the esophageal hiatus.

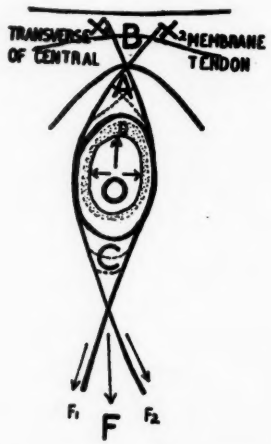

Fig. 3.—Diagrammatic illustration of the forces which tend to widen the esophageal hiatus and of the anatomic structures which oppose such disruption.

The disrupting force (*O*) is the intraperitoneal pressure which constantly tends to force the cardia through the hiatus and so widen the opening. This force is resisted by the construction of the hiatal mechanism.

F, Line of force exerted by the direction of pull of the hiatal muscles $X_{1\text{-}2} - F_{1\text{-}2}$.

A, Action of the anterior decussating muscle fibers which tether the anterior extremities of the hiatal limbs.

B, Transverse membrane which supports the anterior muscle fibers and so buffers the force of the intraperitoneal pressure.

C, Posterior intertendinous muscle (Fig. 7). These fibers tether the hiatal muscles behind the hiatus.

D, Esophagophrenic ligament which acts as an elastic anchor to the terminal esophagus within the hiatal canal.

THE RELATION OF THE ESOPHAGUS TO THE HIATUS

Under normal conditions the stomach cannot be displaced into the mediastinum. The restraining structures are the phrenoesophageal ligaments (described by Schatzki,[18] Anders and Bahrmann,[3] and Roux[17]) and an aggregation of posterior structures which include the vagus nerve and radicles of the left gastric vein and artery.[4]

The phrenoesophageal ligament is a definite structure. It is best developed where the terminal esophagus traverses the hiatus, extending for about a centimeter above the gastroesophageal junction. Above diaphragm level it thins

rapidly and merges with the perivisceral fascia of the esophagus.[12] Below, the ligament reflects circumferentially to become continuous with the fascia transversalis on the undersurface of the diaphragm. If a finger is introduced into the lumen of the lower esophagus, the anterior reflection of the phrenoesophageal ligament is felt as a thick cordlike structure. This ligament is readily definable in the young but is less obvious in elderly people and is attentuated and inconspicuous when a hiatus hernia is present.

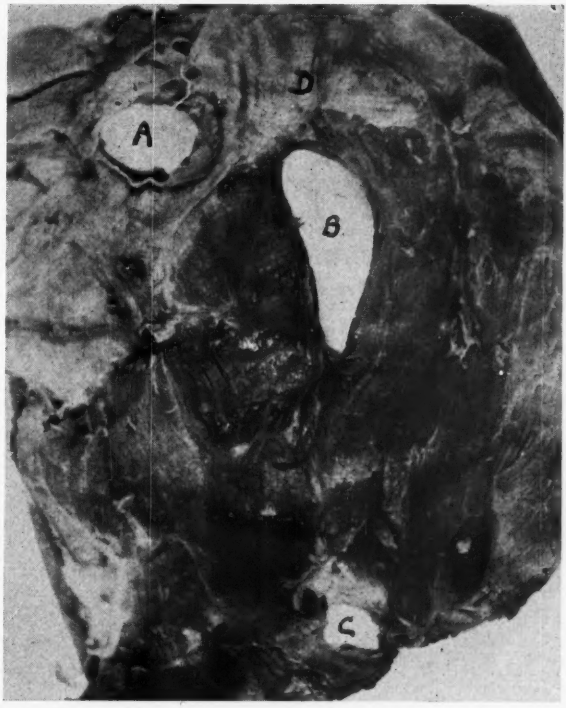

Fig. 4.—Dissection of a diaphragm of standard anatomic pattern viewed from below. The elliptical shape of the hiatus is shown. Note that the anterior margin of the hiatus is separated from the transverse ligament of the central tendon by muscle. (See text.)

A, Inferior vena cava. *B*, Esophageal hiatus. *C*, Aorta. *D*, Transverse membrane of central tendon of diaphragm.

THE HIATAL ANATOMY IN THE PRESENCE OF HERNIATION

Two diaphragms were dissected in people with hiatus hernias who died from unrelated causes. Detailed notes have also been made of the anatomic findings at 58 operations for repair of hiatus hernia.

In the presence of a hernia, the esophageal hiatus usually abuts directly on the transverse membrane of the central tendon and the anterior hiatal muscles are absent or reduced to a few atrophic strands (Figs. 5, 6, and 7). The hiatus itself is no longer a sagittal slit, but a rounded opening whose transverse diameter

Fig. 5.—Dissection viewed from above of diaphragm which was the seat of a hiatus hernia. The hiatus abuts directly on the transverse membrane of the central tendon. The peritoneum herniating through the anterior defect was buttonholed in 2 places during dissection.

A, Inferior vena cava. *B*, Buttonholed peritoneal sac. *C*, Stomach herniated above the diaphragm. *D*, Transverse membrane of central tendon.

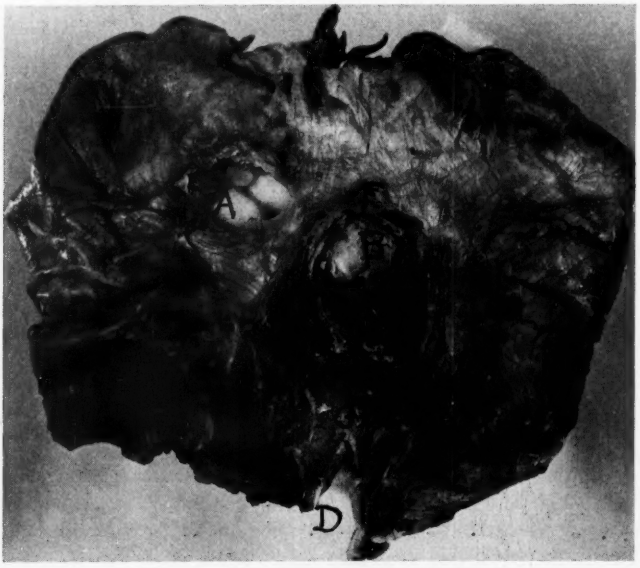

Fig. 6.—Dissection of a diaphragm associated with herniation of the stomach through the esophageal hiatus (viewed from below). The right hiatal limb is reinforced by a slip of muscle from the left crus; a post intercrural muscle is present. Note the rounded opening of the hiatus and the absence of muscle fibers lining the anterior rim of the opening.

A, Inferior vena cava. *B*, Anterior peritoneal sac. *C*, Stomach. *D*, Aortic opening. *E*, Post intercrural muscle. *F*, Transverse membrane of central tendon of diaphragm. *G*, Muscle band arising from the left crus and passing to the right hiatal limb.

approaches the sagittal diameter in size. The essential anatomic difference between the normal hiatus and that associated with a hernia is the increase in the transverse diameter. Associated with the widened hiatus there is an increased separation of the posterior hiatal limbs so that, in place of the normally acute angle formed by the divergence of the right and left hiatal limbs, an obtuse angle may be present (Figs. 6 and 7). The quality of the crural muscle is often surprisingly good even when a large hernia is present.

Other anatomic changes such as the attenuation of the esophagophrenic ligament, elongation of the posterior gastric vessels, and the development of an anterior hernial sac have been frequently described and are generally accepted (Table II).

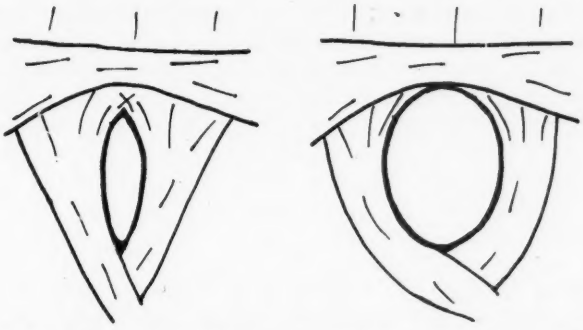

Fig. 7.—Diagram to show the differences between a competent hiatus and one which is the site of a hernia. The anterior rim of muscle is absent, the hiatus is rounded and the hiatal limbs are divaricated posteriorly. The surface area is greatly increased when the hiatus widens and extrinsic support to the cardia is then considerably diminished.

TABLE II. COMPARISON BETWEEN THE NORMAL AND ABNORMAL HIATAL ANATOMY

	NORMAL ANATOMY	HIATUS HERNIA
Size	Admits 1-2 fingers	Admits 3-4 fingers
Shape	Saggital ellipse	Circular opening
Anterior decussating fibers	Present	Absent or atrophic
Posterior muscle bands	"Semi-closed scissor" position	"Open-scissor" position
Hiatal muscle limbs	Generally well developed	Often well developed
Esophagophrenic ligament	Easily definable	Poorly definable
Posterior mesoesophagus (left gastric artery and vein)	Taut	Lax
Anterior peritoneal pouch	Absent or admits finger tip	Admits 2 or 3 fingers easily

DISCUSSION

A previous paper reported a series of experiments designed to measure the forces which the diaphragm has to withstand during life.[15] The pleuroperitoneal pressure gradient constantly tends to extrude the abdominal contents into the

chest and, during deep inspiration and postural change, the pressure may be very considerable. The effect of these physiologic actions is enhanced by pregnancy, obesity, and any other cause of "packing" of the abdominal contents. The intra-abdominal pressure affects the whole diaphragm, but only the esophageal hiatus is vulnerable because it faces directly into the peritoneal cavity. Also, the liver proffers it no protection and its anterior edge is unsupported on the thoracic side. The hiatus transmits the esophagus which does not occupy the opening tightly and which guides the mobile stomach directly into it. The integrity of the hiatus, therefore, depends essentially upon its intrinsic structure where a fine balance between mobility and stability is attained. Competence is primarily dependent upon the size and shape of the hiatus and these are maintained at optimal dimensions by the tethering action of the anterior decussating muscle fibers and the crossover of the crura. So long as the hiatus remains small the hiatal limbs with their membranous reinforcements act as buffers against the positive peritoneal pressure and so protect the esophagophrenic ligament from continuous strain. Most of the intrinsic strength of the hiatus is placed in front of the esophagus. Here the anterior decussating fibers are supported by the transverse membrane of the central tendon and the phrenoesophageal ligament is well developed and cordlike. There is less provision for strength behind where the hiatus is less vulnerable. At the posterior hiatal boundary, the crura are still ascending steeply and are firmly supported by the vertebral column; also, this area is separated from the peritoneum by a cushion of fat and by the extraperitoneal portion of the stomach. Only the anterior ends of the hiatal muscles are therefore exposed to the full force of the pressure exerted from below while distention of the esophagus caused by gastroesophageal reflux tends to widen the hiatus transversely and throw additional strain upon the anterior decussating fibers. If these should disrupt, the hiatus will assume a circular contour, its surface area will greatly increase, and the support for the cardia and the peritoneal reflection will be lost. Once deprived of hiatal support the peritoneum will tend to bulge upward into the mediastinum in front of the esophagus and the phrenoesophageal ligament will now be exposed to the unbuffered force of the intraperitoneal pressure. Should this ligament stretch, as it inevitably must, the cardia will displace upward into the mediastinum. Occasionally the phrenoesophageal ligaments and the left gastric vessels retard the cardia while the gastric fundus rolls into the peritoneal sac. In this way a para-esophageal hernia forms, but this is simply a variant of the sliding hernia. In my experience, it is excessively rare for a "rolling" hernia to be unaccompanied by some degree of upward slide of the cardia.

This concept of the pathogenesis implies that adult hiatus hernia is an acquired malady. This view is supported by the age of onset of the condition. Allison[2] has stated that symptoms characteristically develop in the fifties. We have records of 25 men and 40 women who could clearly recall when first they experienced troublesome dyspepsia and the average age of onset of symptoms in the men was 44 and in the women 42. Rigler and Eneboe,[16] Evans and Bouslog,[8] Dutton and Bland[7] and many others feel that, in many cases, pregnancy is an

etiologic factor. Of our 54 women patients only 2 had never been pregnant and 46 of the remainder (92 per cent) could recall severe symtoms of flatulent dyspepsia during their pregnancies. It is believed that flatulent dyspepsia is invariably due to gastroesophageal regurgitation and that this reflects weakness or strain of the gastroesophageal "sphincter" mechanism.[14] Conditions during pregnancy would seem to be ideally conducive to the development of hiatus herniation. As the gravid uterus enlarges, the abdominal contents are compressed and a pronounced rise in the basal intraperitoneal pressure results. In addition, a profound physiologic effect is exerted upon the collagenous components of the body by a circulating hormone derived from the corpus luteum and placenta. Softening of the collagen in membranes, ligaments, and muscles results and they then tend to stretch in the face of the high abdominal pressures of pregnancy and labor. Rigler and Eneboe[16] subjected 195 women, chosen at random, to barium meal examinations during the third trimester of pregnancy and were able to demonstrate hiatus hernia in 5.1 per cent of primiparas and 18.1 per cent of multiparas. They re-examined 10 patients after parturition and in 4, hernias were still present. These results are highly significant particularly in view of the rigidity of their radiologic criteria for diagnosis and the inadequacy of their technique. During their examinations they made no attempt to raise the abdominal pressure except through coughing and straining. Such actions do not increase the pleuroperitoneal pressure gradient markedly[14, 15] and after parturition, when the abdominal wall is lax, it is necessary that an artificial method of increasing the intraperitoneal pressure should be used before the existence of a hernia is excluded.[12] It is probable that more of Rigler and Eneboe's patients would have shown hernias postnatally had a compression appliance been used. The author has seen 3 multiparous women in the late stages of pregnancy who experienced intractible vomiting caused by hiatus hernias. In each case the persistence of the hernia was confirmed with the aid of sustained abdominal compression from 3 to 6 months after parturition.

Many hiatus hernias must go unrecognized during pregnancy because symptoms of gastroesophageal regurgitation are disregarded, even by the medical attendant. It is true that the symptoms regress after parturition but they tend to recur with subsequent pregnancies or with gain in weight. With 4 of my cases, recurrence of dyspepsia has coincided with the development of pathologic abdominal tumors.

One interprets the course of events as follows: During pregnancy the cardia may herniate through the esophageal hiatus as a result of the softening of the restraining membranes and the raised abdominal pressure. Following parturition, the intraperitoneal pressure is suddenly diminished and the softened body collagen starts to involute. It is generally agreed that stability is restored within 6 months but should membranous and elastic fibers be overstretched or ruptured, they never regain their previous strength. If this has happened to the muscle and membrane of the hiatus, full restitution of the stability is unlikely. However, because of the now capacious abdomen with lax abdominal musculature the

regurgitating force has been dissipated and only when the individual subsequently gains weight and increases her abdominal pressure, do dyspeptic symptoms recur.

Another important etiological factor is obesity. This, by causing "packing" of the abdominal viscera particularly if good abdominal muscle tone is retained, may so raise the basal intraperitoneal pressure as to overcome the intrinsic stability of the esophageal hiatus. We have kept records of the recollected age, height, weight, and basic build of 25 male and 40 female patients at the time when first they experienced symptoms of reflux dyspepsia. With this data it is possible to estimate the ideal weight for a given age and body build. The standard tables recommended by the Metropolitan Insurance Company[19] have been consulted for this purpose. The results of analysis indicate that a high proportion of patients with hiatus hernia first develop dyspepsia when they are overweight. Only one woman (2 per cent) was below ideal weight while 73 per cent were significantly heavier than desirable and 34 per cent were obese. There were fewer obese men in the group but the percentage who were more than 10 per cent above ideal weight was approximately the same as the women (65 per cent and 73 per cent). Among the men who were overweight, there were many who were of powerful build rather than fat. This is too subtle a distinction to analyze statistically, but the strong impression remains that men who retain good abdominal muscle tone are subject to hiatus hernia when they put on weight. It is not suggested that the first symptoms of reflux dyspepsia indicate the presence of a hernia. One agrees with Donnelly[6] that symptoms of flatulent dyspepsia may precede the development of herniation by many years, but it is considered that the causes which produce gastroesophageal regurgitation will also eventually disrupt the esophageal hiatus.

Although pregnancy and obesity are the two common causes of hiatus herniation, they are not necessarily the only ones. Any cause of weakening of the anterior muscle and membrane of the hiatal mechanism may result in herniation. Congenital deficiencies, trauma, or the degeneration of senility could all be responsible. Long-continued increase of the abdominal pressure caused by pregnancy, obesity, abdominal tumors, pyloric spasm, and constricting garments, by exerting an intractable strain upon the exposed anterior edge of the hiatus, may also eventually disrupt the hiatus. In many cases, both basic factors, namely an increased herniating force and a weakened defensive mechanism, will be simultaneously responsible.

Treatment, to be rational, must be directed either toward repair of the anterior defect and the accessory ligaments or to reduction of the herniating force. The first can only be accomplished surgically and the latter medically unless a pathologic tumor is present. Weight reduction can never cure a hernia, yet, by lessening gastroesophageal regurgitation, it may so reduce the symptoms that nothing further need be done. The effectiveness of a pronounced diminution of the regurgitating force is unquestionable, as is instanced by the disappearance of symptoms of reflux dyspepsia after parturition. However, it is believed that once the complications of reflux esophagitis or fundal ulceration are present

one's decision as to treatment should be biased in favor of surgical repair. It must be remembered that the intra-abdominal pressure is the herniating force, and in order to protect the stability of his repair a surgeon is wise to insist upon pre- and postoperative weight reduction.

SUMMARY

1. Thirty diaphragms have been dissected. The anatomy of the esophageal hiatus of the diaphragm is described.

2. The reasons for the susceptibility of the hiatus to herniation are analyzed. It is concluded that stability is dependent upon the narrow size and oblique shape of the hiatus. The crossover of the crural limbs, the decussating muscle fibers, and the transverse membrane of the central tendon of the diaphragm are the major protective structures in that they maintain the size and shape of the hiatus at optimal dimensions. The phrenoesophageal ligament tethers the cardia at diaphragm level but once the hiatus dilates it becomes subject to the full strain of the peritoneal pressure and inevitably it will stretch.

3. The intraperitoneal pressure is the force which tends to produce gastroesophageal regurgitation. The same pressure is also the force which extrudes the stomach into the mediastinum. The effective herniating force is the pleuroperitoneal pressure gradient and this varies physiologically and pathologically. The causes of such variation have been discussed elsewhere.[15]

4. There is a life-long antagonism between the herniating force and the anatomic resisting mechanism of the hiatus. Herniation can occur when the herniating force is increased over a long period of time or when the resisting mechanism is weakened; often both causes are present together. Pregnancy and obesity are the commonest conditions which produce herniation in the adult.

I am grateful to Mr. L. Fatti, Head of the Department of Thoracic Surgery of the Johannesburg Hospital, for allowing me to investigate and treat many of his patients. The illustrations were reproduced by the Photographic Unit of the Department of Medicine, University of the Witwatersrand.

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RECONSTRUCTION OF THE THORACIC AORTA WITH THE AID OF A VASCULAR COUPLING DEVICE (VESSEL COUPLE)

Report of a Case

Timothy Takaro, M.D., and Thomas P. Crymes, M.D.,** Oteen, N. C.*

To CIRCUMVENT the dual problems of spinal cord ischemia and cardiac strain attendant upon occlusion of the upper descending thoracic aorta during reconstructive surgery, intraluminal[1, 2, 3] and extraluminal[4-7] shunts, hypothermia,[8, 9] and extracorporeal circulation[10, 11, 12] have all been used with success. Additional techniques have been suggested by the work of Fryfogle and his associates,[13] and by that of Villegas,[14] Kelly and Alden,[15] and Tibbs and Leslie.[16] These surgeons have designed devices which make possible rapid approximation of the opened ends of vessels or of vessels and grafts, with minimal interruption of blood flow. A leisurely suture-anastomosis in a more or less conventional manner is then possible while blood is flowing through the vessels being anastomosed. Subsequently, the devices are removed. A number of nonsuture techniques have also been suggested[17, 18, 19] but, in two of these, the devices are left permanently in the vessel. This is usually not a desirable feature.

An additional technique is presented in this report, based on a new coupling device. After experience with it had been gained with 40 animals in the experimental laboratory, it was applied clinically in a patient with a syphilitic aneurysm of the upper third of the descending thoracic aorta.

The instrument, designed by one of us (T. T.), is essentially a vascular clamp made up of two cylindrical jaws of unequal length, bivalved to permit removal, and carrying fine teeth on one or two apposing ridges.† Two bolts which fit into perforated, slotted wings on the cylinders, make it possible to adjust the distance between the jaws of the clamp, and also to hold together the halves of each cylinder (Fig. 1). The technique of application of the clamps is illustrated in Fig. 2. The important feature to be noted is that the edges of both the vessel and the graft to be anastomosed present themselves between the jaws of the clamp, and are thus available for suturing under direct vision.

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Received for publication April 21, 1958.

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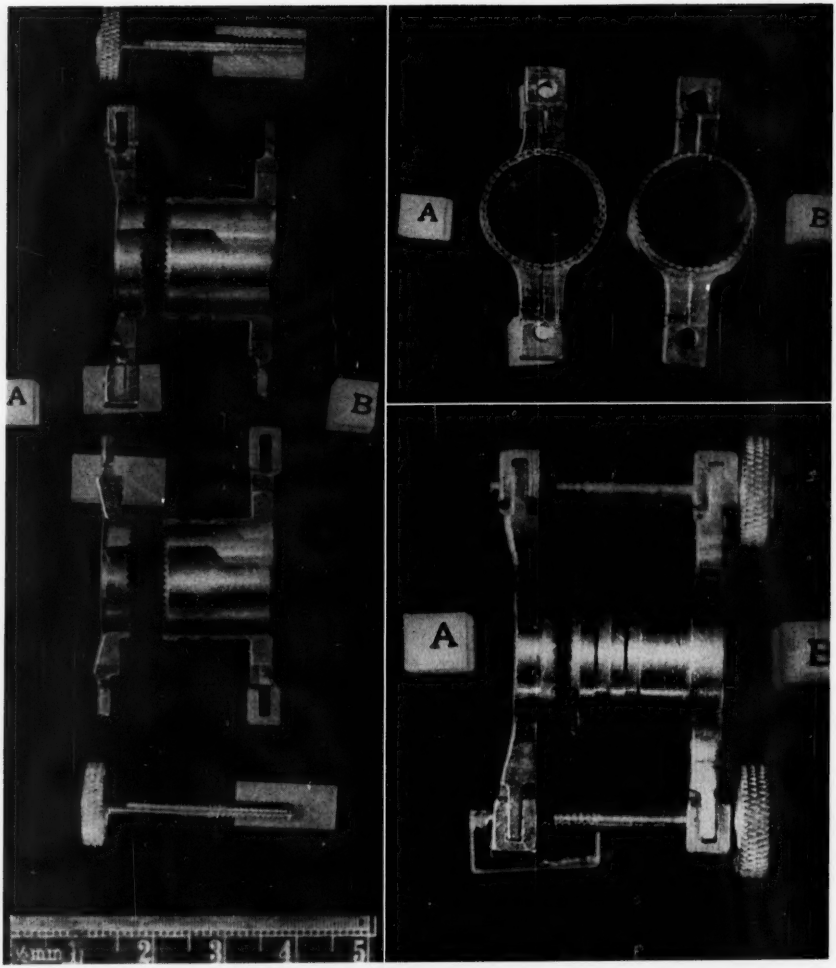

Fig. 1.—The vessel couple disassembled, and assembled.

A, Extraluminal jaw bearing fine teeth on two ridges with V-shaped groove between them.

B, Intraluminal jaw, or graft-bearing portion of couple, bearing fine teeth on a single ridge, which fits into the groove of the opposite jaw. In addition, on the shank of the cylinder there are two square-cut grooves, one to hold a temporary graft-everting ligature, and the other for a temporary wire snare to hold the vessel cuff on the couple until the bolts can be placed. The two bolts adjust distance between jaws, and also serve to hold the halves of each jaw together.

Fig. 2.—Technique of anastomosis using vessel couples.

A, Host vessel prepared to receive graft-bearing portion of vessel couple. The extraluminal jaw is in place around the vessels and held together with temporary ligatures. Stay sutures steady the edge of the vessel. Both of these steps are usually done before blood flow is interrupted. After temporary occlusion of the blood vessel, it is opened over half its circumference. It is not divided completely.

B, Intraluminal or graft-bearing jaw with nylon graft held everted on the couple with a temporary ligature gripping the first groove. This holds the halves of the couple together as well.

C, Host vessel pulled over intraluminal graft-bearing jaw of the couple and held in place with temporary wire snare gripping second groove, until bolts can be put into place and secured.

D, Vessel couple holds vessel and graft securely by multiple fine teeth on interdigitating ridges. The wire snare, the stay sutures in the edge of the vessel, and the ligature holding the graft everted on the intraluminal jaw have all been removed. Blood flow has been re-established, and suturing of the edge of the vessel and the edge of the graft under direct vision has been started.

E, The completed anastomosis—an everting suture line, following removal of the couples. A similar process is ordinarily carried out on the other end of the graft.

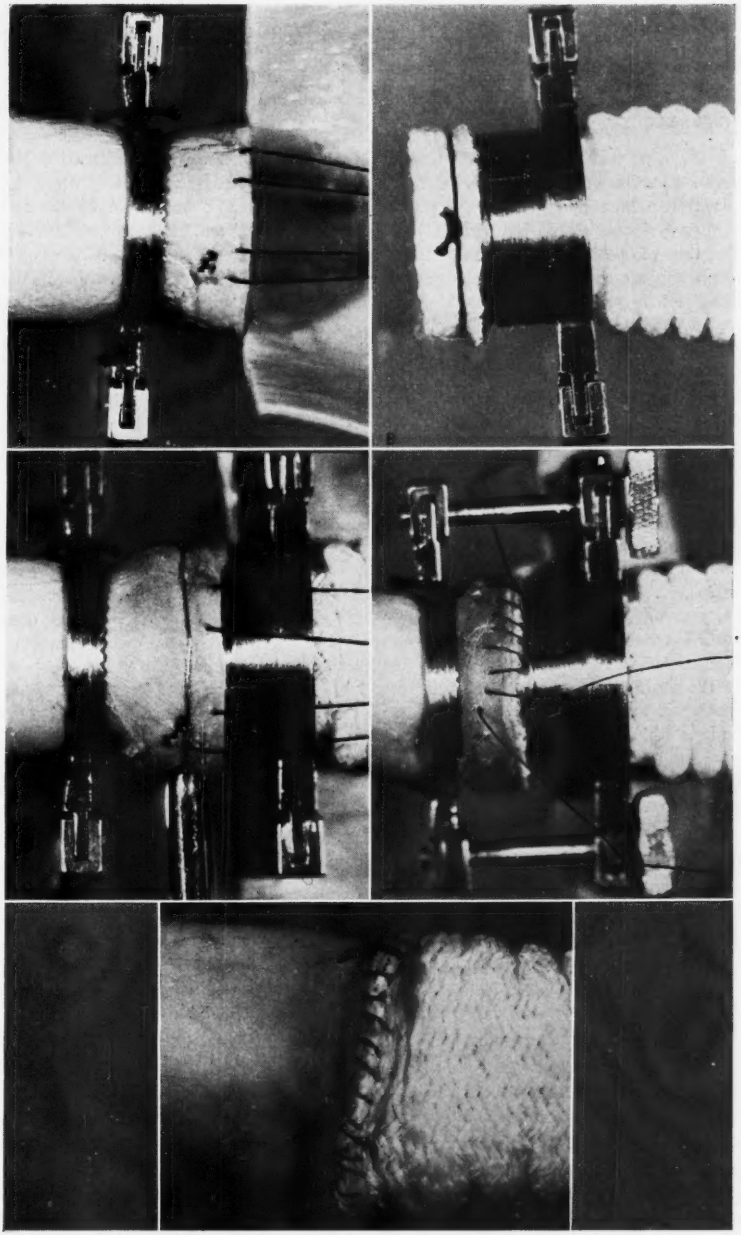

Fig. 2, *A-E.—For legend see opposite page.*

A vessel couple with an internal diameter roughly two thirds to three fourths that of the external diameter of the blood-filled aorta has been found by experience to be about the correct size.

CASE REPORT

R. E., a 64-year-old white man, was admitted to the Veterans Administration Hospital, Oteen, N. C., with a 2-year history of left chest pain. A mediastinal mass, which had not been seen on a roentgenogram of the chest 5 months previously, was noted by the referring attending physicians at the VA Hospital, Beckley, West Virginia. Subsequent investigations revealed that the patient had received treatment for syphilis some 30 years previously; that he had been subject to seizures of the grand mal type during the past 3 years; and that his wife had noted gradual mental deterioration over the past several years. The patient had suffered a cerebral concussion in an auto accident in April, 1955.

The physical examination was not remarkable. A pulsating posterior mediastinal mass was seen at fluoroscopy, and cardioangiography, using a technique described by McCaughan and Pate,[20] showed this to be an aneurysm involving the upper descending thoracic aorta just distal to the origin of the left subclavian artery. Laboratory studies were unremarkable except that the VDRL serological reaction was positive in a dilution of 1 to 64 and the Kolmer was positive 4 plus in both blood and spinal fluid.

Resection of the thoracic aneurysm was carried out on March 7, 1958, through a left posterolateral thoracotomy incision. An 8 by 15 cm. fusosacciform aneurysm originating in a widened portion of the aorta, 1.5 cm. beyond the origin of the left subclavian artery, was dissected almost completely free of the lung, vertebral column, and esophagus. The largest available vessel couple (2 cm. internal diameter) was prepared with a 15 cm. length of specially manufactured Edwards-Tapp crimped nylon fabric tubing, 2.5 cm. in diameter,* for insertion into the aorta distal to the aneurysm. At the site of the distal anastomosis the aorta measured 3.2 cm. in diameter. A larger couple was not available for use proximally where the aorta measured 4 cm. in diameter and, in any event, the short distance between the aneurysm and the origin of the left subclavian artery would not have permitted use of a couple at this point. The aorta was occluded above and below the aneurysm and divided above. An anastomosis between the nylon graft and the proximal aorta was carried out using a simple over-and-over running suture of 4-0 silk. This anastomosis together with some necessary brief dissection after division of the aorta occupied 25 minutes.

The aneurysm was then laid open down to normal distal aorta, around which the extraluminal jaw of the vessel couple had previously been placed. The graft-bearing intraluminal jaw was then inserted into the incompletely divided end of the distal aorta, and held in place temporarily with a wire snare. The bolts approximating the jaws of the clamp were applied and tightened and the occlusive clamps on the aorta above and below the aneurysm were removed, re-establishing blood flow, which was now directed through the graft. These maneuvers occupied 7 minutes. There was considerable hemorrhage through the interstices of the graft despite "pre-clotting" in a basin of fresh blood before use, and marked hypotension for a brief period of time resulted. There was no bleeding between the jaws of the couple.

The aneurysm was next freed completely from its remaining attachments to the distal aorta and the esophagus, and removed. After dividing and removing the temporary ligature which held the graft everted on the vessel couple, the edges of both the aorta and the graft were available for suturing. An anastomosis was carried out between them, using the same simple running over-and-over suture of 4-0 silk. An everting suture-line resulted. The vessel couple was then removed. Bleeding from the anastomosis was minimal. The only feature which marred the final result was rather marked bowing of the nylon graft, due to stretching

*Generously donated by the U. S. Catheter & Instrument Co., Glens Falls, N. Y.

of the prosthesis associated with the large volume of blood flow at high pressure. This made it impossible to cover the graft with mediastinal pleura. The wound was closed, and both pleural cavities drained with negative pressure.

The patient reacted promptly and moved all his extremities vigorously. He was oliguric for 2 days, but thereafter excreted over a liter of urine daily. Blood urea nitrogen rose to 56 mg. per cent on the fifth day, and declined thereafter. Since there was no evidence of damage to the spinal cord, his transient oliguria and azotemia were attributed to the period of hypotension during surgery. The left recurrent laryngeal nerve had apparently been injured by dissection or traction during the operation, and there was hoarseness and aspiration of food and fluids. A tracheostomy was done on the third postoperative day and oral intake stopped. Nevertheless, the patient developed a fulminating bilateral bronchopneumonia due to a hemolytic *Staphylococcus aureus*, resistant to all antibiotics except Furadantin and Magnamycin, and died on the ninth postoperative day.

Fig. 3.—Autopsy specimen showing nylon graft in descending thoracic aorta, which had functioned perfectly for 9 days until death due to staphylococcal bronchopneumonia. The proximal anastomosis, at the top of the photograph, was made in the conventional manner; the lower anastomosis was made with the aid of a vessel couple while blood was flowing through the graft.

An autopsy was done. This showed bilateral suppurative bronchopneumonia, and a small localized empyema at the right anterior thoracotomy site. There was evidence of a mild to moderate nephrosis. The graft was intact and had apparently functioned well. The proximal anastomosis was technically satisfactory and the distal anastomosis was excellent (Fig. 3).

DISCUSSION

Although shunts, hypothermia, and extracorporeal circulation have been used with success in treating aneurysms in this area, serious complications may

accompany the use of all of these methods. Thus, the continued search for other techniques which might be used independently or in conjunction with the three mentioned above.

The technique presented allows the surgeon ample time to anastomose vessels and grafts, the ends of which are under direct vision for suturing while blood flows through the vessels being united. In using the Fryfogle vessel couples, we have been uneasy with the blind suturing method required, and unhappy with our results in the experimental laboratory. These difficulties are compounded with diseased, thickened vessels, and heavy graft material. We have had no experience with the other couples which have been described in the literature.

If a long enough cuff of vessel proximally is not available to allow use of the vessel couple for the definitive graft, by-pass shunts can be placed rapidly with this device, using the left subclavian artery proximally, and the descending aorta distally. After the proximal anastomosis of the definitive graft has been made in the conventional manner, the shunt can be uncoupled distally, and the distal end of the graft coupled to the aorta in its place. Similarly, use of vessel couples in conjunction with hypothermia or extracorporeal circulation might shorten the time of application of these techniques and thus perhaps increase the margin of safety for the patient.

We are currently engaged in the laboratory in replacing the arch of the aorta in dogs and in suturing Hufnagel valves into the thoracic aorta with the aid of vessel couples. These experiments and the details of the laboratory work leading to the development of the technique described in this paper will be reported elsewhere. Modifications of the design of this coupling device, and other applications of this and other devices with similar aims will undoubtedly occur to surgeons interested in this field.

SUMMARY

A technique for reconstructing the thoracic aorta using removable vessel couples of special design, with minimal interruption of blood flow, is described. A conventional suture-anastomosis can be made while blood is flowing through the vessels to be joined, since the ends of the vessels are available between the jaws of the clamp for suturing under direct vision. This technique was successfully applied in reconstruction of the upper descending thoracic aorta in a patient with a syphilitic aneurysm, using a crimped nylon fabric seamless-tube prosthesis. However, the patient died on the ninth postoperative day of a fulminating staphylococcal bronchopneumonia.

We wish to acknowledge the assistance of Mr. Robert P. Ramer of Sangli, India, of Mr. Harry Smith, Miraj, India, and of the Bombay Surgical Company, Bombay, India, in the development of some of the earlier models of our vessel couple.

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PRESSURE MEMBRANE OXYGENATOR

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MANY varieties of artificial pump-oxygenators for total cardiopulmonary bypass have been described. All are variants of one of the main three types: the film,[5, 7, 8] the bubble,[3, 4] and the membrane oxygenator.[1, 3] Each one of these methods of oxygenating blood has its limitations. Common to the first two varieties is the existence of the gas blood interface which has been demonstrated to denature the blood proteins.[2] The membrane oxygenator protects the extracorporeal blood from the gaseous oxygen and prevents air embolization. Its efficiency is limited by the ability of the membrane to allow the exchange of gases between the blood and its ambient medium. This limitation has been partially compensated for by the increase of the membrane surface exposed to the blood.[1] Consequently the size of the apparatus and its priming volume increased.[10] The purpose of this paper is to describe a pressure membrane oxygenator capable of diffusing four times more oxygen than has previously been reported.[1] Thus, the size of the apparatus and its priming volume can be proportionately decreased.

PRINCIPLES

On the basis of the kinetic molecular theory of gases it can be shown that the number of moles (M) of a gas at a given pressure diffusing through a surface (S) of a membrane of a known thickness (Z) during a period of time (T) can be represented by the formula[11]:

$$M = \frac{K \times S \times (P1 - P2)\ T}{\sqrt{Mol.\ Wt.} \times Z}$$

Where K = Constant of porosity of the membrane.
P1 = Pressure of gas on one side of the membrane.
P2 = Pressure of gas on the other side of the membrane.
Mol. Wt. = Molecular weight of the gas.

If, in the above formula, the constants are eliminated the volume (V) of a gas diffusing through the membrane per unit time per unit surface area will

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This investigation was supported by research grants from the National Health Institute, United States Public Health Service, and the American Heart Association.

Received for publication April 23, 1958.

be proportional to the pressure gradient between the two surfaces of the membrane:

$$V \sim P1 - P2.$$

The rate of diffusion of carbon dioxide dissolved in the blood will follow Graham's law and will be proportional to the difference in partial pressure of carbon dioxide on the two sides of the membrane and inversely proportional to the square root of its molecular weight.[6]

It is these principles which have been applied in the construction of the proposed "pressure membrane oxygenator."

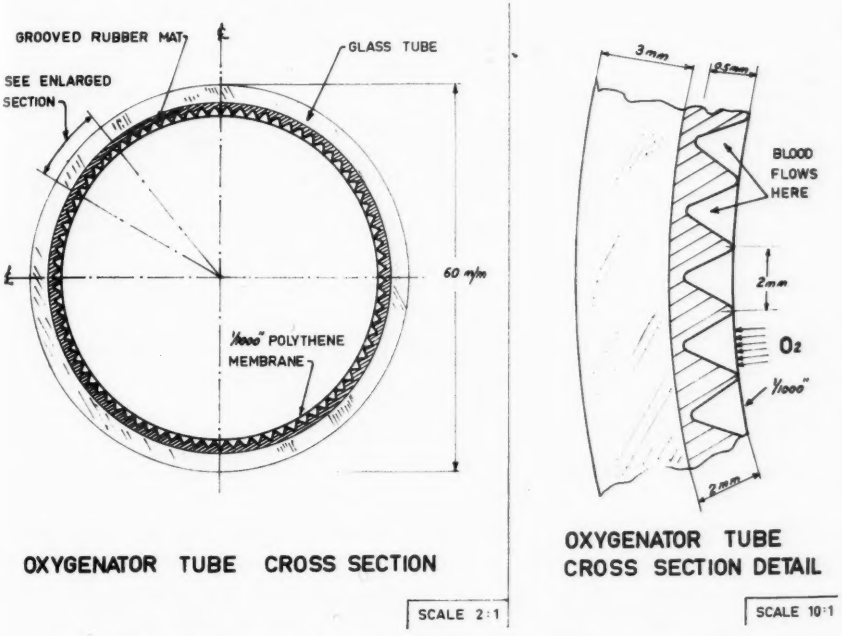

Fig. 1.—Engineering drawing of a cross section at the middle of the oxygenating unit.

MATERIAL AND METHODS

A cylindrical polyethylene (Polythene) membrane 0.00254 cm. (0.001 inch) in thickness was tested against pressure and its rupturing point determined. Its ability to diffuse oxygen and carbon dioxide under a given pressure was measured and compared with the results obtained by other investigators.[1] A measured volume of fresh canine venous blood was circulated around the membrane for a definite period of time. The oxygen and carbon dioxide content of the venous and arterialized blood was determined by the method of Van Slyke and Neill,[13] and the pH was determined with a glass electrode (Beckman pH meter). The pressure and the flow of oxygen through the polyethylene cylinder were regulated and measured by a pressure meter and a flow meter.

The blood pressure in the plastic (Mayon) tubing between the venous head of the Sigmamotor pump and the oxygenating unit was monitored with a mercury manometer. All parts of the setup coming in touch with the blood, except the polyethylene membrane, were siliconized.

PROCEDURES

Pressure Membrane Oxygenator.—A cylindrical polyethylene membrane, 0.00254 cm. in thickness, 4.9 cm. in diameter, and 100 cm. in length, presenting a diffusing surface area of 0.154 M.^{2}, was fastened over a rubber stopper on one end and was introduced into a 100 cm.-long glass tube into which a rubber mat with longitudinal grooves had been placed (a grooved plastic tube would

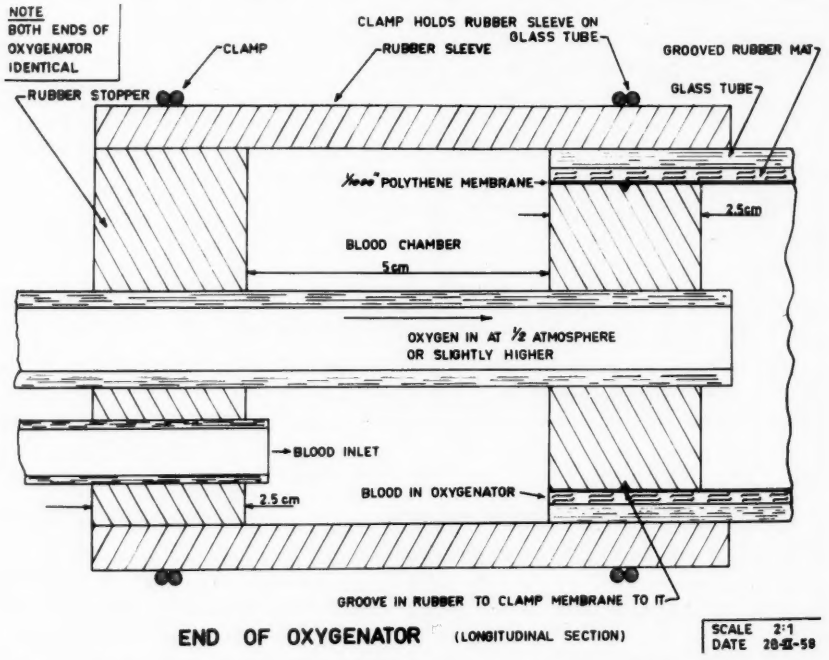

Fig. 2.—Engineering drawing of a longitudinal section at the end of the oxygenating unit.

have been easier to handle). The other end of the membrane was fastened in a similar fashion around another rubber stopper so that all the membrane was supported by the rubber mat. Each of the rubber stoppers had a central hole into which was introduced a 15 cm.-long stainless steel connector. A sleeve of siliconized rubber was fixed to both ends of the outer glass tube and was closed with a rubber stopper with two holes. The central hole admitted the stainless steel connector that had already been introduced into the single hole of the rubber stopper around which the polyethylene membrane was fixed. The other hole admitted a stainless steel connector that directed the blood into and away from the oxygenating unit. A short distance, 3 to 5 cm., was left between the

two rubber stoppers on each end to allow the blood to find its way into and away from the grooves around the membrane (Figs. 1 and 2). The central stainless steel connector on one end was attached to an ordinary oxygen tank with a pressure-reducing flow meter. The central connector on the other end was wired to a rubber tubing with two side-branchings. A Hoffman infusion clamp was applied on one branch and the other branch was attached to a pressure meter. The oxygen flow meter was opened until it marked 8 L. per minute and the Hoffman clamp was tightened until the pressure meter read 500 Gm./sq. cm. At this pressure, the oxygen flow meter usually recorded 3 to 4 L. per minute. Isotonic saline solution was then pumped into the system until all the air was driven out. Four hundred and fifty milliliters of fresh canine venous

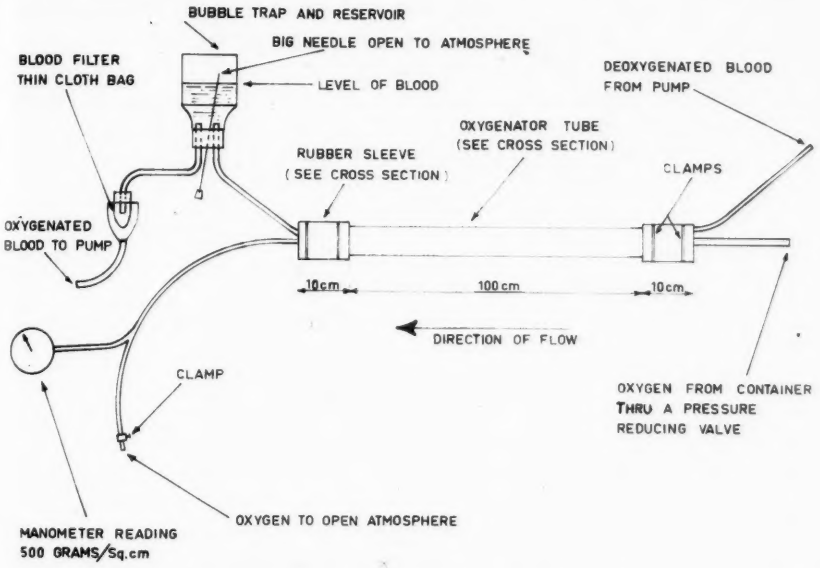

Fig. 3.—Engineering drawing of the general set of one oxygenating unit when assembled.

blood was used to displace the saline solution. The tubes were connected with a stainless steel connector creating a closed system with a bubble trap on the arterial end of the oxygenating unit (Fig. 3). In each experiment the blood was circulating around the membrane for 4 consecutive minutes. Blood samples for analysis were taken at the start and at the end of each perfusion experiment.

RESULTS

The unsupported polyethylene cylinder stood a pressure of 200 Gm./sq. cm. Above this pressure, it dilated and proceeded to rupture. When supported by the grooved cylinder, the membrane stood a pressure of 1,000 Gm./sq.

TABLE I. TABLE OF RESULTS*

EXPERIMENT	VENOUS BLOOD OXYGEN ML. % AND % SATURATION	ARTERIAL BLOOD OXYGEN ML. % AND SATURATION	VENOUS BLOOD (CO_2 mM/L.)	ARTERIAL BLOOD (CO_2 mM/L.)	VENOUS BLOOD (pH)	ARTERIAL BLOOD (pH)	DIFFUSION (ML./M.²/MIN.)	PRESSURE (GM./SQ. CM.)
I	12.74 72.8%	17.42 99.54%	34.8	17.0	7.24	7.3	35.10	500
II	18.24 75%	22.32 93%	34.8	15.1	7.20	7.28	30.0	500
III	19.76 89.94%	21.97 100%	15.26	14.64	7.30	7.40	Bubble formation	500
IV	20.73 94.3%	21.97 100%	14.45	13.8	7.28	7.35	Bubble formation	500
V	14.4 60%	18 75%	31.0	14.64	7.26	7.34	53.3	1,000
VI	14.22 59%	17.82 74%	32.0	13.8	7.22	7.34	53.3	1,000

*Four hundred and fifty milliliters of blood was circulated for 4 minutes around a surface area of 0.154 M.² of a polyethylene membrane, 0.00254 cm. in thickness.

cm. At this pressure, however, the membrane wedged itself into the furrows of the mat. The resistance to the circulating blood was thus increased and the pressure in the plastic tubing between the venous head of the pump and the oxygenating unit reached 360 mm. of mercury. At this same pressure, the diffusion of oxygen through the membrane was 53.3 ml./M.^{2}/min. At a pressure of 500 Gm./sq. cm. the pressure of the blood between the venous head of the pump and the oxygenating unit was 180 mm. of mercury. At this pressure the oxygen diffusion averaged 32.5 ml./M.^{2}/min. The carbon dioxide content of the venous blood averaged 27.05 mM/L. and that of the arterialized blood 14.49 mM/L. The pH of the arterialized blood went up to 7.33 ± 0.01 as compared with 7.25 ± 0.01 for the venous blood.

In another set of experiments in which blood with a relatively high oxygen content (19.76 V per cent, 89.94 per cent saturated, and 20.73 V per cent, 94.30 per cent saturated) was used, it was found that the blood became fully saturated (21.97 V per cent) and fine bubbles appeared in the tubing system. These results are presented in the accompanying table (Table I).

DISCUSSION

The crests of the grooved mat over which the polyethylene membrane lies not only support the membrane, preventing it from rupturing at a pressure of 500 Gm./sq. cm., but also prevent it from wedging into the grooves. Thus, the blood will pass through the grooves around the membrane and pick up the diffused oxygen without having the pressure inside the membrane transmitted to it.

The diffusion of oxygen across the membrane is directly proportional to the pressure gradient between the two surfaces of the membrane (P1 – P2). Whereas at atmospheric pressure 7.6 ml. of oxygen was reported to diffuse across one square meter per minute, at a pressure of 500 Gm./sq. cm. above atmospheric pressure an equal surface of a membrane of the same thickness and chemical composition diffused 32.5 ml. of oxygen per minute. This represents an increase in diffusion efficiency of 427 per cent. At a pressure of 1,000 Gm., the diffusion efficiency became 705 per cent. At such a high pressure a thicker membrane is less likely to wedge into the grooves and the blood will circulate without any increase in the resistance to its flow.

In the experiments in which the circulating blood could not dissolve and combine with all the diffused oxygen, the formation of homogeneously distributed microbubbles was noticed. The bubbles represent the increment of oxygen diffused over the oxygen dissolved in, and combined with, the blood. From these experiments it is concluded that the volume of blood circulating around the membrane should have the ability to dissolve and combine with all the oxygen diffused in order to prevent the formation of bubbles. The formation of these bubbles can be prevented either by increasing the circulating blood volume (and this is limited by the volume of the venous return), or by decreasing the

pressure inside the membrane. As an added safety measure a bubble trap has been included in the circuit to allow the escape of such bubbles and to act as a reservoir for blood.

The carbon dioxide elimination was very effective. Although the pressure inside the membrane was 500 Gm./sq. cm., the partial pressure of carbon dioxide was zero and its elimination from an average of 33 mM/L. in the venous blood to 14.6 mM/L. in the arterial blood is the result of the high pressure gradient between the two surfaces of the membrane. In spite of the high rate of carbon dioxide diffusion the pH of the blood did not change appreciably. It went up from 7.24 ± 0.01 to 7.33 ± 0.01. This low carbon dioxide content plus a normal pH is similar to a state of compensated respiratory alkalosis which can be prevented by mixing carbon dioxide with the oxygen in order to decrease the pressure gradient of carbon dioxide.

In order to have a diffusing surface large enough to provide a sufficient amount of oxygen to saturate all the venous return, several oxygenating units can be assembled in parallel. This arrangement increases the "mechanical efficiency" of the system by increasing its surface of diffusion and decreasing its total resistance to the blood flow according to the following formula derived from Poiseuille's law[12]:

$$\frac{1}{R} = \frac{1}{R_1} + \frac{1}{R_2} \cdots + \frac{1}{R_n}$$

Where R = total resistance

R_1, R_2, R_n = respective resistance of each oxygenating unit.

SUMMARY AND CONCLUSIONS

A pressure membrane oxygenator has been described. The oxygen diffusion through a polyethylene membrane 0.00254 cm. (0.001 inch) in thickness, at a pressure of 500 Gm./sq. cm. above atmospheric pressure, was found to be 32.5 ml./M.²/min. and, at a pressure of 1,000 Gm./sq. cm., it was found to be 53.3 ml./M.²/min. This represents increases, respectively, of 427 per cent and 705 per cent in the diffusion efficiency of a similar membrane at atmospheric pressure. In the method described enough blood should circulate around the diffusing membrane to dissolve and combine with all the diffused oxygen in order to prevent the formation of microbubbles. The carbon dioxide elimination was effective and the pH of the blood did not change appreciably.

I wish to express appreciation to Professor Thomas Bridgewood of the Faculty of Engineering, American University of Beirut, for the engineering drawings, and to Mrs. K. Hemadeh for the chemical analysis of the blood specimens.

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CILIARY STREAMING THROUGH THE LARYNX AND TRACHEA

Relation to Direction of Ciliary Beat and Significance in Sites of Respiratory Disease

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THE PATTERN of flow of the mucous blanket from the bronchial tree through the larynx is so designed as to avoid the squamous epithelium covering the vocal cords.[1] Drainage, on the way to the esophagus, is directed through the interarytenoid area.[2] This region is covered by ciliated epithelium. Lower in the bronchial tree, the openings of tributary bronchi act as obstructions in the ciliary stream and these, like the vocal cords, must be bypassed.[3]

Are the curving patterns of flow around these obstructions due to directions of ciliary beat, other than the usual axial one, or, are they due only to unequal, oblique traction upon a tenacious mucous blanket? The present study was undertaken to answer this question. Observations were made of the patterns of flow about the natural obstructions and about artificial obstructions interposed in three different areas: (1) in the trachea, where the ciliary stream flows straight and axial and where the ciliary beat is presumably in the long axis of the air passage; (2) at the carina tracheae where the mucous blanket makes a four-way split and changes direction sharply, and (3) upon the vocal cords, where there is a split of the blanket and a right-angle change of direction.

One cannot avoid wondering if these patterns of flow are related to the distribution of disease in the respiratory tract.

The material used in this study consisted in tracheas removed from freshly killed cows and the larynges and tracheas removed from freshly killed calves.

The specimens were kept, until used, in plastic bags to prevent drying. It was unnecessary to warm the specimens above room temperature to preserve ciliary activity.

The technique was the same as that used in previous studies.[1, 3, 4, 5] The tracheal specimens were split in the midline posteriorly, spread out and nailed or pinned to boards. Some of the laryngeal specimens were similarly split and others were halved by cutting in the midline anteriorly and posteriorly. India ink, placed upon the mucous blanket, was watched in its progress along the ciliary stream.

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Supported by grants from the Louis W. and Maud Hill Family Foundation of St. Paul, the Edward C. Congdon Memorial Trust, Miss Elisabeth Congdon and the Women's Service Guild of St. Luke's Hospital.

Received for publication April 25, 1958.

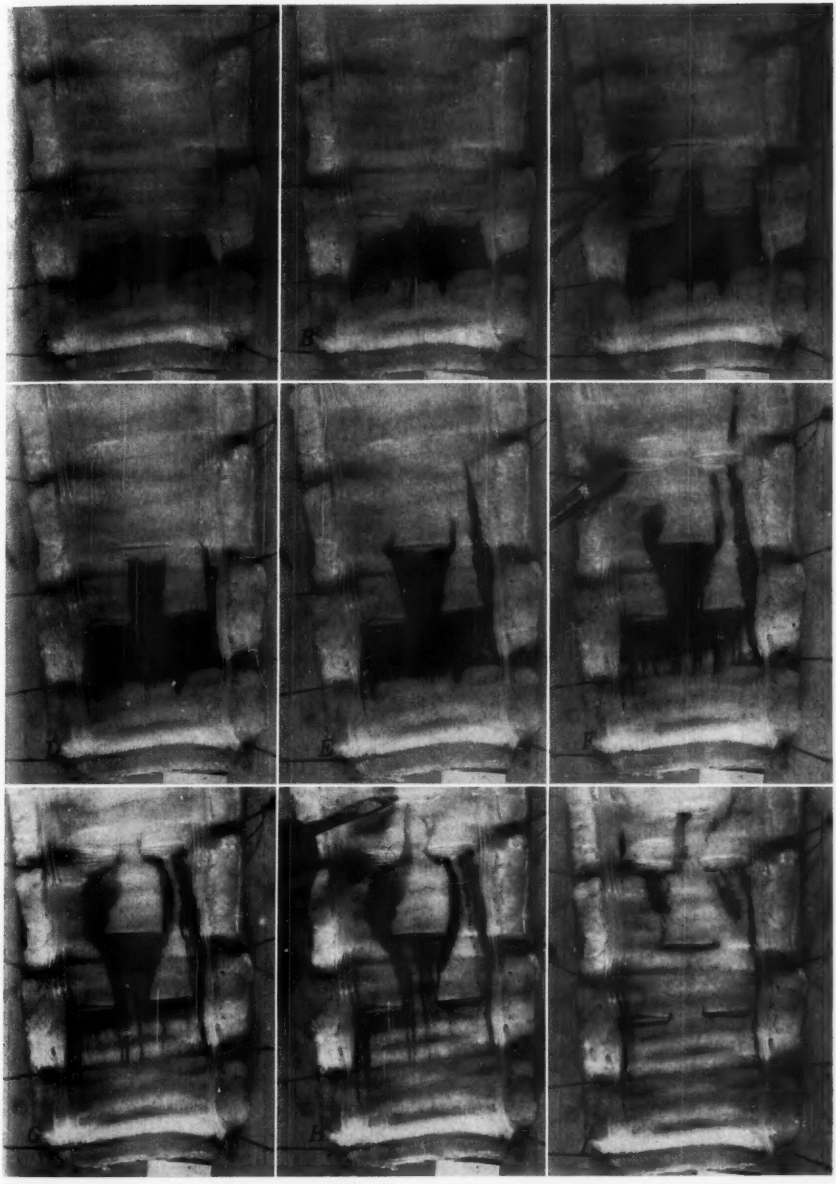

Fig. 1.—Trachea of calf showing ciliary streaming about six serially made transverse incisions placed in a pattern. The winding course can be readily appreciated by following the central stream through the series. This course is presumably due to unequal traction upon the mucous blanket. Each incision dividing the blanket removes downstream traction from the area immediately upstream, thus reducing the velocity here. Three orders of velocity are apparent: (1) that of uninterrupted flow, (2) that on the upstream side which can be seen by comparing the flow in the right-hand and central streams in *C*, *D* and *E*, and (3) that on the downstream side of the incisions (seen in the right-hand stream in *F* and *G*).

Tracheal Incisions.—Incisions (straight, curved and circular, placed transversely and obliquely) were made through the mucous blanket and mucous membrane in sections of the tracheas of cows in imitation of the natural obstructions, for the purpose of determining the effects of traction upon the mucous blanket and the behavior of the latter at such obstructions.

Transverse: The pattern of flow about single and multiple transverse incisions was found to be rather characteristic, with variations in detail depending upon the viscosity of the blanket and the positions of the incisions relative to one another and to the long axis of the air passage.

It is to be remembered that the ciliary stream in man is upside down. "Downstream" is upward toward the larynx and conversely "upstream" is down toward the alveoli.

Fig. 2.—Calf trachea showing residual ink-stained mucus pushed into transverse incisions by ciliary action. The second incision from the top was filled to the point where it made contact with the blanket on the downstream side, thus re-establishing drainage.

When India ink is placed upstream from a transverse incision, it flows toward the incision and, at a variable point upstream, some of it begins to deviate toward one or both ends of the incision (Fig. 1). Flow directly toward the incision continues but more slowly than the prongs passing around the ends. The latter may pass the ends of the incision and already be far up the trachea (downstream) before that which is flowing directly toward the incision arrives at its upstream margin. Arriving there, this portion collects and overflows into the incision—a phenomenon that can be explained only by a direct push by the underlying cilia, since the factor of traction at this level has been removed by the division of the mucous blanket. Not infrequently the accumulation in the incision may become so great that it spans the gap, makes contact with the mucous blanket on the downstream side and once more starts off toward the upper trachea (Fig. 2). When the area has cleansed itself of ink, a residuum always remains in the incision.

When a number of incisions are laid out in a pattern, as shown in Fig. 1, the phenomenon of traction and different velocities gives a meandering pattern such as that illustrated. The portions which flow axially are obstructed at the incisions, which they fill more or less completely, and in which a residuum remains when the rest of the mucosa has cleaned itself.

Oblique, inverted "L," and circular incisions: Oblique, inverted "L," and circular incisions were made and the pattern of flow was similar to that described at the transverse incisions, with some variations in detail. In each instance a residuum remained at the upstream margin of the incision.

Axial: Axial incisions did not cause a deviation of flow nor an accumulation of ink. The ink-stained mucus flowed parallel with the incisions on both sides and there was no tendency to overflow the margins.

Curved: Very striking and illuminating were the patterns formed about curved incisions with the concavity directed upstream (Fig. 3). Deviating prongs first flowed past the two horns of the crescents, as past the straight, transverse, or oblique incisions. Later the flow filled in the concavity to the upstream lip of the incision and also the blanket dragged past and over the two horns, as it was pulled downstream by traction.

Fig. 3.—Pattern of flow about two curved incisions. Even though the factor of traction has been eliminated within the concavity by the incision, the ink travels to and overflows the upstream margin. This action is due to the ciliary beat.

When the blanket is less viscid, the deviation of flow is less marked. If the blanket is first largely washed away with Ringer's solution, then the flow is almost entirely parallel with the long axis of the trachea and the ink gathers in the incisions with little tendency to flow about the ends. This would seem to indicate that considerable tension may develop in the original mucous blanket under certain circumstances.

Laryngeal Experiments.—The preceding experiments with obstructing incisions in the trachea indicate that, by virtue of traction on the mucous blanket, drainage about obstructions was rather good, even though the ciliary beat was axial in direction. It was not perfect because invariably some residual ink remained at the upstream margin. It is conceivable that drainage about the vocal cords could be explained on the basis of traction alone in the presence of axially

beating cilia in surrounding areas. It would be more effective if the direction of ciliary beat were that of the direction of flow rather than axial. Several experiments were done to determine the direction of beat in the region just inferior (caudad) to the cords.

Axial incisions: In an experiment done on 6 cows and 2 calves, an axial incision was made through the posterior part of the vocal cord and then ink placed low in the anterior larynx or across the entire circumference in the upper trachea or lower larynx. If the ciliary beat had been axial in direction upon the lateral wall and cords, the ciliary flow should then also have been axial in direction, flowing parallel with the incision on both sides, as it did in the trachea; but this it did not do.

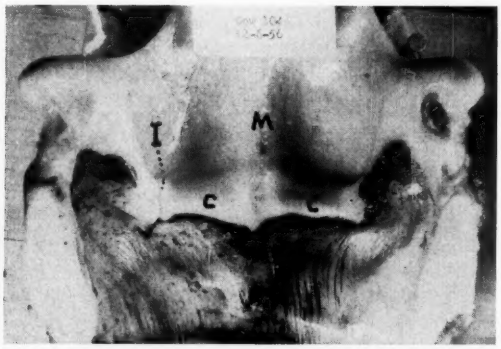

Fig. 4.—Larynx of cow split in midline posteriorly and spread to show the interior. *C* = vocal chords. *M* = Midline anteriorly. *I* = Axial incision across posterior end of vocal cord. This incision eliminated the factor of traction at this line but the oblique directions of flow were not altered indicating that the direction of ciliary beat just below the cords is not axial but oblique.

Four of these larynges were split in the midline posteriorly, spread out and nailed to a board. The incision was made through the mucous blanket and mucous membrane across the arytenoid and posterior part of the left cord. The right side acted as the control (Fig. 4). A line of ink was allowed to flow across the entire circumference of the lower larynx and the larynx placed in an upright position, so that streaming would be upward against gravity. The flow was sluggish in some, but, in general, was about symmetrical on the two sides, flowing up and posteriorly upon the lateral walls to avoid the cords. That upon the anterior half of the left side flowed to the anterior lip of the incision and then overflowed into the incision; that in the posterior half rose posterior to the incision and then flowed away from this in an upward and posterior direction.

Four larynges were divided completely into right and left halves by midline incisions, both anteriorly and posteriorly, and the two halves mounted separately in three and only the left half in the fourth. In 1 (Cow 93), the ink flowed posteriorly and around the inferior end of the incision in the left half. The right was used as a control and showed the usual up and back flow. In another, the flow on the left lateral wall described a spiral course flowing first

anteriorly and upward, then swinging posteriorly under the cord to pile up at the anterior margin of the incision (Cow 74). The right half (control) exhibited the same odd anterior, upward and posterior spiral. In the other 2, the flow was up and back to the anterior lip of the incision. In 1 of these (Calf 43), the axial incision was made in both halves. In the right half, the ink-stained mucus filled the incision, made contact with the blanket on the posterior side and was pulled across. Streaming was too sluggish in the left to carry the ink as far as the incision.

These experiments all seemed to show that the posterior flow on the lateral wall of the larynx was not due to traction on the blanket because the flow in that direction continued even when the possibility of traction from the interarytenoid area had been removed by the axial incision. Moreover, the fact that ink-stained mucus collected on the anterior lip of the incision, and never the posterior, indicated that the incision lay across the direction of ciliary beat.

Isolation of subglottic region: A rectangle of mucous membrane lying just caudad from the vocal cord was isolated by the axial incision just described and a transverse incision running anterior from this to the midline and parallel with the cord and at the level of the cricoid cartilage. This isolated rectangle was bounded by the midline anteriorly, the axial incision posteriorly, the transverse incision inferiorly, and the squamous epithelium of the cord, superiorly (By "superior" is meant cephalad and "inferior," caudad.) Ink was placed at the anterior-inferior corner of the rectangle and its progress observed.

This experiment was done in the larynges of 6 calves. In 5 of these the larynx was split open posteriorly and mounted upon a board with the anterior aspect dependent and the upper end raised somewhat. The left was used as the test side and the right as control. In the sixth, the larynx was completely divided in the midline anteriorly and posteriorly and only the right half used in the test.

In all 6, the direction of flow from the anterior-inferior corner in the isolated rectangle was up and back. Anteriorly it was almost straight up but inclined progressively more and more posteriorly as the arytenoid was approached, until just beneath the arytenoid, it was more back than up. The pattern was symmetrical on both sides but, in some, there was a little more motion on the control side where traction also was effective. Ciliary flow was sluggish in all and, in 3 the ink did not carry as far as the axial incision, but, in the other 3, it flowed to and over the anterior lip of the incision. This experiment also indicates that the ciliary beat in the subglottic region is not axial in direction.

Visualization of Ciliary Beat.—Many attempts were made to visualize the cilia to determine the direction of beat.

Direction of beat in larynx: The wave fronts were seen in a fair number of laryngeal specimens. The wave front ordinarily lies at right angles to the plane of beat and progresses in the direction of beat. The wave fronts in these specimens progressed along curved lines, passing up and back in much the same pattern as the lines of flow.

The left half of the larynx of Cow 124 was irrigated and then stained lightly with India ink. The cilia could be seen fairly well and the direction of ciliary beat just under the cords anteriorly was axial and toward the cord at about right angles but, under the posterior portion of the cords, the direction of beat was posterior and up.

Five hemilarynges from 3 calves were mounted on blocks and chilled in the refrigerator until the cilia slowed and almost stopped. When examined under a dissecting microscope, the direction of beat could be visualized quite readily. A sixth half exhibited such slow ciliary action that the direction of beat could be observed without refrigeration.

In these six hemilarynges, the direction of beat in the subglottic region was axial and toward the cord anteriorly but, progressing toward the arytenoid, inclined more and more backward. Just under the latter it was up and back at about 45 degrees.

Direction of beat in trachea: It has been assumed in these studies that the plane of ciliary beat in the trachea was parallel to the long axis. To verify this, long sections of the tracheas (a third to a half of the full length) from 3 calves were split posteriorly, spread open, mounted on boards and chilled in the refrigerator to slow the ciliary movements sufficiently so that they could be followed. Many fields were examined in each and, with one exception, the beat was parallel to the long axis of the trachea in all 3. In one specimen, in a single field, near the margin of the incision along the posterior wall, where the mucosa was thrown into folds, the beat seemed to be some 15 to 20 degrees off the long axis.

It is conceivable that the direction of ciliary beat might be altered in some way by incisions in the trachea, such as those described above. Therefore, the direction of beat was studied about some of these incisions after chilling and there was no evidence found that the direction had been altered. It remained axial in all fields examined.

DISCUSSION

These studies indicate that the plane in which the tracheal cilia beat is generally parallel with the long axis of the trachea. This, of course, would be expected. Artificial obstructions to ciliary streaming, in the form of variously placed incisions, show no evidence of a change in the direction of ciliary beat.* But the ciliary stream, in these freshly killed cows and calves, deviates more or less to avoid such obstructions, and much of it bypasses. The flow is faster in those portions that deviate than in those that flow directly to the obstructing incision. This would seem to indicate that the blanket in the latter area has been deprived of some of its motivating power, as though there were a downstream pull in the blanket that has been lost by cutting across the blanket.

*This is consistent with the recently reported findings of Beattie and Correll[6] in reversing a section of trachea while making studies pertinent to a surgical graft of certain portions of the trachea. These workers reversed large sections of trachea in dogs and chickens. They found, as far as the epithelium was concerned, that it all degenerated and disappeared with the exception of islands of replacement cells next to the basement membrane. From these, the epithelium was eventually completely restored by new cells. In the new cells the direction of ciliary beat was the same as that of those lost. In the reversed graft they beat in a caudad direction.

Since the blanket is viscid and will sustain traction, this downstream pull is effective past the ends of the incision and upstream, thus causing the observed deviation. How much, if any, tension develops in the blanket of the normal, living bronchial tree is problematic. How well the blanket would be maneuvered about similar obstructions in the living is unknown. It is known that the nonciliated areas in the nose are drained by traction.

Under certain conditions, the flow of the ciliary stream may be greatly retarded or cease entirely, although the underlying cilia may continue to beat vigorously. Threads of mucus that remain attached within the glands that produced them often extend downstream for considerable distances and are attached to the underside of the mucous blanket. These act as anchors that retard or stop the progress of the blanket even when the cilia continue to beat rapidly.

It could be possible that drainage of mucus about naturally occurring obstructions, such as the bronchial openings, and the vocal cords, is accomplished through traction alone by cilia that beat in an axial direction. This is not the case, however. At both the bronchial openings and the vocal cords, the cilia beat obliquely, to push the blanket past these obstructions. This was demonstrated at the major and minor carinae in a previous study.[5] It was shown to be the case at the vocal cords by the experiments with incisions, as described above, as well as being demonstrated by direct vision after slowing the ciliary beat by chilling. The direction varies between the anterior commissure and the arytenoid cartilage from an axial one at the commissure to an oblique one of about 45 degrees just under the arytenoid.

The epithelium on the margin of the cords is squamous in type, whereas that in the interarytenoid region is ciliated. Practically all mucus normally drained from the lower tract passes out between the arytenoids, the major portion flowing there directly without ever reaching the cords. It is at the cords, however, especially in the anterior portion, that a slowing of drainage takes place. The blanket coming to the anterior commissure and anterior part of the cords approaches at right angles, since the cilia here are beating in an axial plane or nearly so. Here, at the anterior cords, it ceases its axial progress, is torn asunder into two parts, each of which turns at right angles to flow backward under the margin of the cords.

Incomplete studies on human larynges seem to show a pattern like that in these animals inferior to the cord. What it is like above the cords, I cannot say at this time. The bovine animal does not have a ventricle or ventricular band, nor does it have a ventricular appendage, which in man is richly supplied with mucous glands. In man, certain squamous islands often occur in the bronchial tree, especially in the main bronchi. The manner of ciliary flow about these has not been demonstrated but, if traction upon the blanket plays the same role as elsewhere, and it presumably does, then the blanket would flow partly over and partly around such spots with perhaps some retardation of velocity.

One cannot avoid wondering what relation, if any, this pattern of flow has to the distribution of disease in the respiratory tract. Carcinoma occurs most frequently at the margin of the cords and in their anterior half. Tuberculous

lesions occur characteristically in the interarytenoid area. Why should this difference obtain? I do not think the answer is known, but one is tempted to speculate. Speculation is perhaps permissible as long as one keeps clearly in mind exactly what he is doing.

One possible explanation might be about as follows: An invasion and infection of a spot of tissue by the tubercle bacillus theoretically is a single event. Theoretically, it would be possible for a single organism to initiate a lesion. Since laryngeal lesions are comparatively uncommon in pulmonary tuberculosis, it must be, from the viewpoint of the bacillus, an exceedingly rare occurrence; perhaps it could be compared with the fertilization of the ovum by a sperm cell. This event seems to be purely a matter of chance with a single ovum involved and millions of sperm cells swarming about. This also is a single event. Since practically all of the drainage from the lower respiratory tract passes between the arytenoids, the number of tubercle bacilli passing here would be greater than elsewhere in the larynx, and other factors being equal, the likelihood of invasion would be correspondingly greater—hence the distribution of tuberculous lesions.

As information becomes available concerning the initiation of carcinoma, the indications are that an entirely different process is involved than in the case of the tubercle bacillus. Carcinoma in the larynx is presumably not caused by a single event, rather by the repeated application of certain carcinogenic compounds over long periods of time. The time element plays a big role—not only must the application be repeated a great many times over many years, but each application to a given spot presumably must be of a certain minimal duration. Thus, carcinoma would seem prone to occur at some point where the flow of the ciliary stream, bearing the carcinogenic materials, is retarded more or less. Such an area could be the anterior portions of the cords, where the mucous blanket ceases its axial progress and must be torn in half to pass at right angles in different directions, and this is actually where carcinoma does occur most frequently.

Although the bronchial tree is not the subject of this study, reference has been made to previous studies concerning ciliary streaming and possible modes of carcinogenesis in this portion of the respiratory tract. It might be of interest to point out that carcinoma of the bronchial tree tends to occur in the root of the lungs and that this distribution can be explained on the basis of retardation of ciliary flow. It is in this region that the squamous islands are prone to occur and it is here that numerous large bronchial openings act as obstructions.[3, 4, 7] In the trachea there is usually no obstruction to flow and carcinoma here is infrequent.

CONCLUSION

1. These studies in the larynges of animals indicate that the pattern of ciliary streaming is so designed as to avoid flow across the vocal cords. Eventually practically all of the drainage from the lower tract passes through the interarytenoid region.

2. The observed directions of flow in the larynx are due to a combination of oblique traction upon the mucous blanket and oblique planes of ciliary beat.

3. In the trachea both the ciliary beat and the direction of ciliary streaming seem to be parallel to the long axis of the trachea.

SUMMARY OF SPECULATIVE COMMENT

One can speculate as to the relation these findings might have to the distribution of disease. Tuberculous lesions occur commonly in the interarytenoid area, where the flow of tubercle bacilli reaches its greatest concentration. Theoretically, a tuberculous infection is a single event and, other things being equal, would occur where the concentration of bacteria is the greatest.

On the other hand, carcinogenesis seems to involve many insults of minimal duration repeated frequently over a long period of years. These conditions would prevail where the mucous blanket is retarded in its flow. Such an area would be at the level of the vocal cords, at or near the midline anteriorly, where the mucous blanket ceases its axial progress and is torn asunder to flow at right angles in opposite directions. Actually this is where carcinoma of the larynx is most apt to be found.

Carcinoma of the bronchial tree is prone to occur in the root of the lung, where there are large obstructing openings from tributary bronchi, and where squamous islands are apt to occur. Carcinoma rarely occurs in the trachea where the ciliary streaming is free and uninterrupted.

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THE METABOLIC EFFECTS OF AN INTRATHORACIC STOMACH ON A GROWING CHILD

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For many years, surgeons have sought the ideal method for restoring gastroesophageal continuity in extensive lye strictures of the esophagus. Sweet,[11] in 1946, described the technique of subtotal esophagectomy with high intrathoracic esophagogastric anastomosis for the treatment of extensive cicatricial obliteration of the esophagus, which was a major advance over methods previously available. In 1951, Paine[7] reported 2 cases of lye stricture in children who underwent successful esophagogastrostomy. Other reports of similar successes with this operation in infants and children are now comparatively common.

While there has been much discussion as to the possible adverse effects that might occur from an intrathoracic stomach in infants and children, no studies of this nature have been reported in the American medical literature. An intrathoracic stomach is known to be poorly tolerated by the infant during the first 6 months to 1 year of life; thereafter, the problem of acute respiratory distress is of less concern. However, to our knowledge, the effects of a total intrathoracic stomach on growth and development have not been completely documented. Consequently, this paper presents a careful evaluation of the metabolic effects on 2 children with intrathoracic stomachs.

The 2 patients studied were a boy now 13 years of age (M. S.) and a girl now 16 years old (N. H.). Both had intractable lye strictures and underwent esophagectomy with high esophagogastrostomies* 8 years ago.

The cardiorespiratory, hemopoietic, and gastrointestinal systems were evaluated in this study. A careful history and physical examination with special attention to the above-mentioned areas was done, as well as electrocardiogram, pulmonary function studies, chest x-ray, and hematologic work-up.† The gastrointestinal tract was evaluated in relation to the child's growth and development as plotted on the Wetzel Grid.[12] Motility of the intrathoracic stomach was

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Supported by the Wood and Brooks Fund.

Received for publication April 30, 1958.

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†Hematologic studies were performed by Dr. Clair Shumway, hematologist at Buffalo Children's Hospital.

studied by recording pressures from intragastric tubes and the contour and emptying time of the stomach by barium x-ray studies. Studies included a gastric analysis, Hollander test to determine the presence or absence of vagal innervation. Complete metabolic studies for absorption of carbohydrate, fat, and protein were performed to determine any altered effects due to the intrathoracic stomach.

CARDIORESPIRATORY EVALUATION

Both children had frequent respiratory infections during the first 1 to 2 years following the esophagogastrostomy. Since then, however, this complication has been no more frequent than in normal children. This fact, plus the lack of chronic cough and sputum production, is highly suggestive that there is no postprandial or nocturnal aspiration. Of interest is the persistent presence of dyspnea and fullness in the chest for 1 to 2 hours following the ingestion of larger than normal meals.

Significant physical findings reveal normal contour and expansion of the thorax with no evidence of kyphoscoliosis. Auscultation of the chest was essentially normal. However, musical expiratory râles were noted on occasion in M. S. during episodes of seasonal asthma which this boy has been known to have in the past few years.

The chest roentgenograms were within normal limits. The only abnormality was fullness at the right border of the mediastinum due to the intrathoracic stomach. Electrocardiogram was within normal limits.

Predicted normal pulmonary function cannot be as accurately estimated in children as in adults. However, it is recommended by Ferris and co-workers[1, 2] that these values be based upon age, height, weight, sex, and body surface rather than on only one of these aforementioned factors. The following figures represent the predicted norms of pulmonary function, using Ferris's standards, with the observed values of each child.

Predicted According to:	*Vital Capacity*		*Maximal Breathing Capacity*	
	N. H.	M. S.	N. H.	M. S.
Age	3.27L.	3.48L.	92.0L.	92.0L.
Height	3.41L.	1.82L.	107.3L.	68.0L.
Weight	2.73L.	1.50L.	97.6L.	53.0L.
Body Surface	2.83L.	1.73L.	93.0L.	65.0L.
Observed:	2.60L.	1.37L.	133.0L.	81.0L.

The vital capacity observed in these children fell below predicted normal limits. However, the maximum breathing capacity was well within the normal range. The spirogram pattern of both children showed no abnormalities whatsoever; even the boy (M. S.), who has moderately severe asthma, had no evidence of air trapping. The disparity between the low vital capacity value and the normal maximum breathing capacity is the result of the space-occupying effect of the intrathoracic stomach which lowers the vital capacity. This is particularly significant since these respiratory studies were performed in the fasting state.

HEMATOLOGIC EVALUATION

The results of the hematologic studies on N. H. revealed a normal hemoglobin, hematocrit, white blood cell count, and differential count. The serum iron concentration was 170 gamma per cent. The examination of the blood smear revealed that platelets were present in adequate numbers, and that the erythrocytes exhibited some hypochromia. The alterations of erythrocyte morphology in N. H. were undoubtedly the result of the previous splenectomy done at the time of esophagogastrostomy. Similar studies on M. S. were within normal limits except for an eosinophilia of 19 per cent, which is compatible with his known allergic asthma. The examination of the blood smear revealed that platelets were present in adequate numbers, and that the erythrocytes were normal in appearance.

GASTROINTESTINAL TRACT EVALUATION

After the early compensatory period of 1 to 2 years following the esophagogastrostomy, these children have had relatively normal eating habits. Both of them have excellent appetites and eat three full meals a day and often, after the evening meal, will take a bedtime snack. It is of interest that one of these children (N. H.) can vomit if she so desires; the other child (M. S.) finds that voluntary emesis is impossible even if he so desires. Neither child has had any symptoms suggestive of esophagitis, such as heartburn or substernal pain. M. S. does have some eructation following meals, while N. H. does not. N. H. experiences regurgitation of sour fluid after meals if she lies flat while M. S. does not have this difficulty.

The effects of the thoracic stomach on the growth and development of these children was of major interest (Fig. 1). The growth of these children has been interpolated on to a modification of the Wetzel Grid.[12] The curve of N. H. lies near the median norm both prior to her lye burn and also during the period of esophageal dilatations and gastrostomy feedings. Following her esophageal resection, her growth continued to stay within the area normal for her until the second year following surgery, during which time it slowed rather markedly. This drop can be accounted for by repeated respiratory infections and several bouts of pneumonia during this period. Since then, however, she has had no serious illnesses and her growth curve has return to its previous norm. Today there is no evidence of impairment of growth in this child and the bone age by roentgen examination is likewise normal.

M. S. presents a somewhat more complicated problem. His pre-lye burn and post-lye burn growth area lies within normal limits. However, following his surgery, the curve became subnormal and has remained so, a sign of a definite growth impairment. This is substantiated by the fact that his bone age is also retarded by 2 years. The cause of this impaired growth is somewhat difficult to evaluate, since it could be due not only to the effects of the intrathoracic stomach, but also to the fact that this child is a severe asthmatic during the late summer and fall seasons, which in itself could greatly interfere with his normal growth.

Ingestion of barium by both patients showed normal peristaltic activity on fluoroscopy and complete evacuation of the stomach within 1 hour. It was of interest that a rapid emptying time of the stomach was observed in both patients because only a modified pyloroplasty was performed on M. S. and no pyloroplasty was done on N. H. The intragastric pressure studies were performed by having the subject swallow three fine polyethylene tubes, fused together, which were used to measure pressure from the intrathoracic stomach at the diaphragmatic and midthoracic levels and from the esophagus within the apex of the chest. Pressures from each tube were recorded simultaneously through Statham strain gauges on a multichannel recorder. A lateral hole was made near the distal end of each tube beyond which the tube was filled

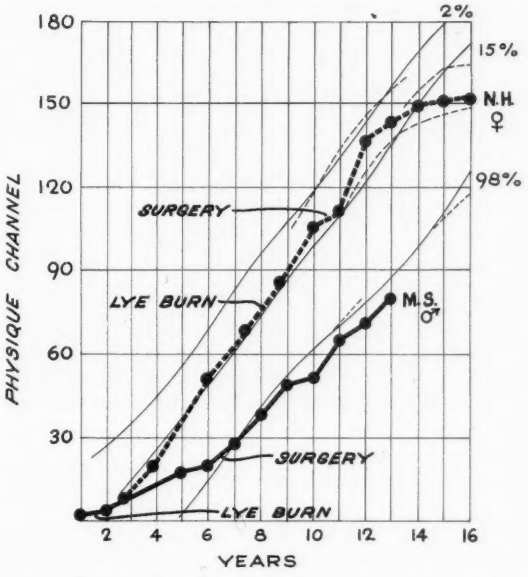
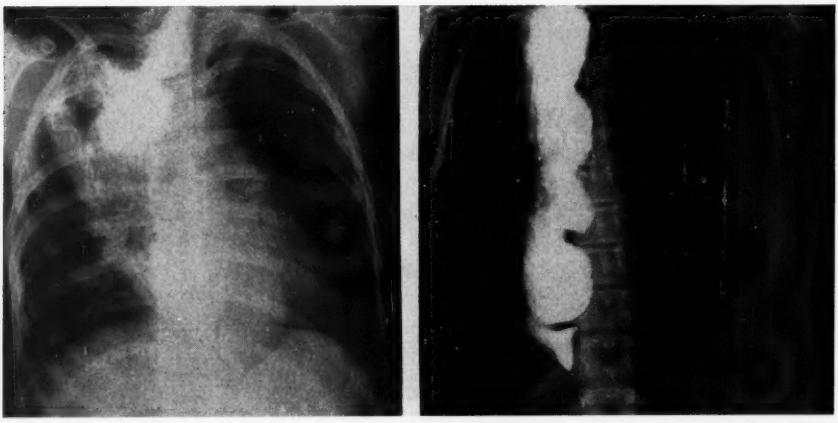


Fig. 1.—Modified Wetzel Grid showing growth and development curves (see text).

with mercury to permit its localization by roentgenography. Recordings were made during quiet and deep respirations, coughing, and with manual abdominal pressure in supine and lateral positions. The negative intrathoracic pressure changes were readily transmitted through all three tubes during quiet and deep respirations. Each tube showed positive pressure waves with coughing. Moderate increase in abdominal pressure by manual compression was not reflected through the intrathoracic tubes despite the disturbed anatomy at the diaphragmatic hiatal area from the previous surgery. When the major part of the stomach remains within the abdomen and there is loss of the normal gastroesophageal competence as with hiatus hernia or low supradiaphragmatic esophagogastrostomy, the positive upper abdominal (intragastric) pressure may be transmitted

to the distal esophagus. At irregular intervals, large positive pressure deflections, apparently from gastric contractions, were recorded from the two intragastric tubes.

Careful evaluation of the position and contour of the intrathoracic stomach using barium contrast medium demonstrated that it lay entirely within the chest in both children. This organ showed a remarkable ability to accommodate over the years to the new position within the thorax. This is illustrated by Fig. 2, which shows a barium study approximately 1 month postoperatively in N. H. and a subsequent study 7 years later. The fundus of the stomach, which once occupied the entire right chest, now lies as a tubular structure adjacent to the mediastinal border.



A. *B.*

Fig. 2.—Barium swallow following high intrathoracic esophagogastrostomy (N. H.). *A*, One month postoperative. *B*, Seven years postoperative. Note change in contour of stomach.

Because of the altered position of the stomach and the surgical section of the vagus nerves, studies were done to determine the vagal control of gastric secretions and the presence of hydrochloric acid. The two tests used for this purpose were the fractional gastric analysis with histamine stimulation of the stomach and the Hollander insulin test.[4]

The gastric acidity was determined by the method described by Roth and Bockus.[8] This test revealed both children to have free acid and the stomach to respond in a normal fashion to histamine stimulation.

The Hollander test, which was used to determine regeneration of the vagus nerves divided at esophagectomy, showed that there was no response to insulin induced hypoglycemia in either child. This indicates that there is no vagal control over the gastric secretion of hydrochloric acid and that, consequently, no regeneration of the vagal nerve fibers has occurred.

Alterations in carbohydrate, fat, and protein absorption have been described in the literature following gastrectomy or operative procedures which bypass

the stomach. No information, however, is available concerning the above-mentioned alterations of absorption in children with thoracic stomach. It was our desire to see if these metabolic functions were disturbed by the total displacement of the stomach from the abdomen to the chest.

The response of the blood glucose level to the oral administration of sugar was utilized as a measure of carbohydrate absorption. After ingestion of a specified amount of glucose, capillary blood sugar levels were taken at regular intervals using the method advocated by Nelson[6] and Somogyi's[10] modifications. Both patients had normal fasting blood sugar levels. Within 30 minutes, there was an extremely high hyperglycemic phase, indicating a surprisingly low tolerance or rapid absorption of carbohydrate (Fig. 3). This type of glucose tolerance curve is often present in gastrectomized patients with the so-called

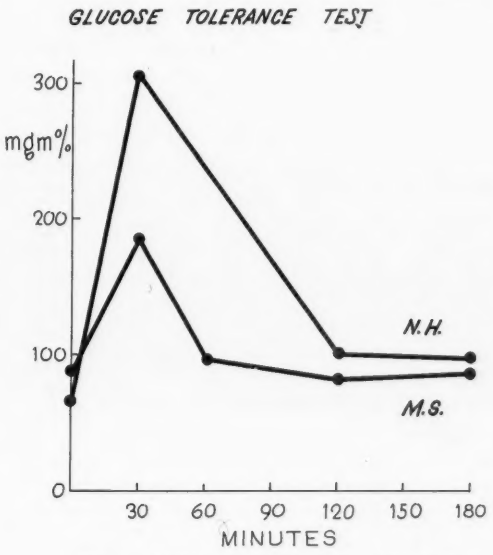


Fig. 3.—Glucose tolerance curves (see text).

"dumping syndrome" and was believed by Glaessner[3] to be the reason for this symptom complex. Although these children showed this "dumping syndrome" type of glucose tolerance curve, neither child had any of the symptoms commonly associated with this entity. The extremely early high blood sugar levels in these patients are interpreted as being an indication of the rapid and complete transit of the ingested glucose through the stomach, and does not indicate any defect in mucosal absorption.

Although there is no generally accepted adequate test available for fat absorption, the most widely accepted current procedure for a qualitative determination is the Vitamin A tolerance test. The method used in our study was that advocated by May and his colleagues.[5] Both children had extremely flat Vitamin A absorption curves (Fig. 4) which is significant in that this type of

curve is noted in most sprue-like syndromes. Since fat metabolism is dependent not only on specific enzyme systems but also on the mechanical efficiency of the gastrointestinal tract, it can be postulated that possibly this defect is the result of incomplete mixing of food materials due to the rapid evacuation from the stomach.

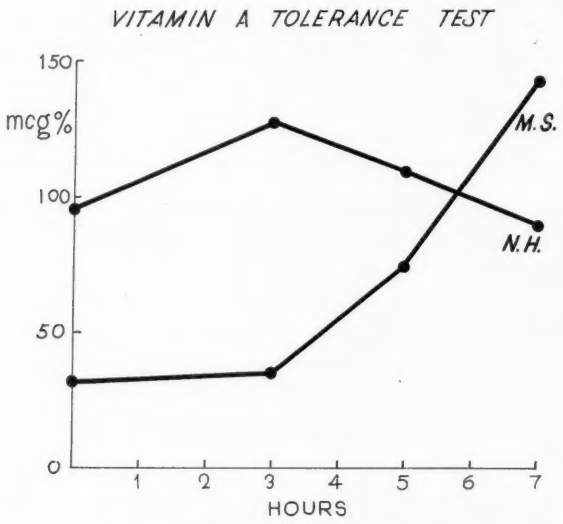


Fig. 4.—Vitamin A absorption curves (see text).

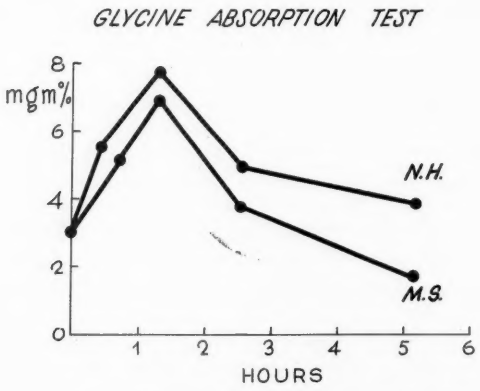


Fig. 5.—Glycine absorption curves (see text).

The ability of the gastrointestinal tract to absorb protein is best studied by determination of one of the specific amino acids rather than the complex protein molecule. The method selected to determine protein absorption was that described by Schwartz and co-workers,[9] in which specific amounts of glycine

were ingested and the plasma glycine content then determined. The results of these tests are shown in Fig. 5. Protein absorption is entirely normal in both children.

Electrophoretic determinations of the serum protein fractions were also done. All the elements of the serum protein were within normal limits except for an extremely high gamma globulin level noted on both children. The reasons for this elevated gamma globulin are obscure and its significance is questionable.

DISCUSSION

It is generally agreed by those familiar with the problem that an intrathoracic stomach is poorly tolerated by infants and young children. This impression was certainly confirmed by the clinical course of our 2 patients during their first 2 postoperative years. During this time, they had repeated respiratory infections and moderate dyspnea following large meals; this latter complaint necessitated frequent small meals during the early postoperative period. However, these troublesome complications abated after several years. The manner in which the stomach compensated for these symptoms could be demonstrated by x-ray studies which showed that it changed from a sigmoid-shaped organ into a straightened tubular structure, thus allowing the lungs to have more space in the thoracic cage. While these patients clinically have no evidence of respiratory insufficiency, they have vital capacities which are below the normal for children of similar size, age and sex, but their maximum breathing capacities are normal. This is best explained by the space-occupying effect of the intrathoracic stomach.

Another interesting phenomenon associated with the intrathoracic stomach in these 2 children is the rapid emptying time of the stomach, which is demonstrated by the barium meal and also suggested by the extremely high blood glucose level 30 minutes after ingestion of glucose. This type of curve is characteristically associated with the so-called "dumping syndrome" following gastric resection. It was of interest to us, however, that neither of these children had any of the common symptoms usually seen with the "dumping syndrome." Another alteration of metabolism that was noted was a rather flat Vitamin A absorption curve in both children. The significance of this is not understood, but it can be stated that both children had curves which are seen in states associated with steatorrhea. Possibly this may be related to the rapid transit through the stomach which prevents complete breakdown of food material so that the intestinal enzymes do not have the properly prepared material on which to act. Although food passes rapidly through the stomach, there appear to be no apparent alterations in peristaltic activity. This was observed both on fluoroscopic examinations and also inferred from the intragastric manometric studies.

A definite loss of the cardioesophageal spincter mechanism was confirmed by manometric studies, as might be expected. However, so far there have been no clinical symptoms suggestive of esophagitis, although esophagoscopy is the only way definitely to rule this out. It seems less likely that these children

will develop esophagitis from gastroesophageal reflux in the future as long as the stomach continues to empty rapidly and the esophagus is not exposed to acid-pepsin secretions.

The general systemic effects of a thoracic stomach noted by us are somewhat difficult to interpret. One patient, N. H., has perfectly normal growth and development, as shown both by her Wetzel Grid curve and also by bone development. The other child, M. S., has impaired growth both on the Wetzel Grid and by bone age. However, this child also has severe allergic asthma, which may be a contributing cause of his poor growth and development.

SUMMARY

The studies on these 2 children, now 8 years following high intrathoracic esophagogastrostomy for lye strictures, show certain deficiencies previously discussed. The advantages of relieving the tremendous social and economic burden associated with repeated dilatations and gastrostomy feedings by gastroesophageal anastomosis are most gratifying. It would appear that an intrathoracic stomach can be tolerated with only minor disturbances in metabolic functions. Whether this procedure will prove to be a more desirable method when compared with jejunal or colon transplants for re-establishing gastroesophageal continuity awaits the test of time.

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ESOPHAGEAL OBSTRUCTION DUE TO MEDIASTINAL GRANULOMA

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THE PRODUCTION of esophageal obstruction by mediastinal granuloma has received scant attention in the literature. Both the rarity of these lesions and the confused state of our knowledge relative to their pathogenesis have contributed to this situation.

The first recorded instance of operation for esophageal obstruction due to a mediastinal granuloma appeared as a case report from the Massachusetts General Hospital in the *New England Journal of Medicine* in 1945.[3] The patient had been operated upon by Dr. Richard H. Sweet. Only 5 additional cases have been recorded up to the present time, 3 of them by Garamella, Stutzman, Varco, and Jensen.[1]

Symptoms of esophageal obstruction were encountered in a minority of the reported cases of mediastinal granuloma collected from the literature in 1955 by Garamella and his associates. Dysphagia had been present in only 6 of the 39 cases of mediastinal granuloma managed by operation which were reviewed by them. Other symptoms encountered in some cases of mediastinal granuloma included dyspnea, cough, chest pain, odynophagia, and fever. Sixteen of the 39 patients had been free of symptoms and had been operated upon because the existence of a more serious type of mediastinal tumor could not be ruled out. Although the number of reported cases is limited, the recording of 16 cases of mediastinal granuloma from the Mayo Clinic by Kunkel and his associates[2] and the recent report of 12 cases from the National Naval Medical Center at Bethesda by Peabody and his associates[6] would seem to indicate that the occurrence of mediastinal granuloma may not be as infrequent as the scarcity of reported cases might suggest.

The etiology of the mediastinal granuloma in the majority of the reported cases has been obscure. In some of the early reports, the lesions were classified as tuberculomas. However, as more cases were recorded, the unsuitability of this classification became increasingly apparent. Tubercle bacilli have seldom been identified in these cases and the bacteriologic yield from the culture of

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Supported by a grant from the James Whitcomb Riley Memorial Association.
Received for publication June 2, 1958.

these granulomas has been uniformly negative. In this regard, it is of considerable interest that Peabody and his associates, in their recent report, found 5 of 12 mediastinal granulomas to be due to histoplasmosis. They found that 2 additional patients had positive skin tests to histoplasmin but that the granulomas removed from these patients were histologically negative for *Histoplasma capsulatum.*

The purpose of this paper is to report a case of esophageal obstruction due to a subcarinal mediastinal granuloma in a 43-year-old woman with symptoms of increasing dysphagia and pain. The patient was managed successfully by extramucosal resection of the granuloma. A patch of fine-mesh nylon was utilized for esophageal support in the area of resection in which only a markedly attenuated mucosal remnant remained to cover the lumen of the esophagus.

CASE REPORT

The patient, a 43-year-old white housewife, was admitted to the Ball Memorial Hospital on April 27, 1955, because of difficulty with swallowing and recent roentgen demonstration (as an outpatient) of esophageal obstruction. She had noticed increasing difficulty with swallowing during the 4 weeks prior to her admission to the hospital. Her swallowing difficulties were accompanied at times by a feeling of substernal fullness and back pain. Initially her troubles were limited to the ingestion of solid foods. However, by the time of her admission to the hospital, she was also experiencing difficulty with liquids. On April 16, roentgen study of the esophagus with orally ingested barium had been carried out. A small diverticulum was demonstrated on the right lateral wall of the middle portion of the esophagus. The diverticulum measured approximately 1 cm. in diameter and emptied readily. About 2 inches below the diverticulum, in the subcarinal area, a nonopaque, ovoid filling defect in the esophagus was identified (Fig. 1). Thick barium was retained at this level. There was no esophageal dilatation above this area of partial obstruction. The mucosal pattern of the esophagus did not appear to be disturbed by the obstructing mass.

The patient had been healthy throughout her life up to the onset of her present illness. There was no history of exposure to tuberculosis. The findings on physical examination were essentially within normal limits. The admission red blood count was 5.1 million with 16.5 grams of hemoglobin. Her white blood count was 6,200 with a differential count of 2 per cent eosinophils, 2 per cent basophils, 40 per cent lymphocytes, 9 per cent monocytes, and 47 per cent neutrophils. The urine examination was within normal limits. Two days following her admission to the hospital, the roentgen study of her esophagus with barium was repeated. The findings confirmed the observations made 13 days earlier. There was no change in the appearance of the esophageal obstruction. On April 30, esophagoscopy was carried out. The lumen of the esophagus appeared to be completely obstructed at the approximate level of the radiologically demonstrated obstruction. The esophageal mucosa which covered the obstructing mass was intact and appeared to be normal. No effort was made to biopsy this mass through the intact esophageal mucosa or to thrust the esophagoscope past the obstructing mass. On the basis of the esophagoscopic and roentgen findings, a tentative diagnosis of benign extramucosal esophageal tumor, most likely leiomyoma, was made.

On May 2, the patient was taken to the operating room and a right lateral thoracotomy was carried out under general, endotracheal anesthesia through the bed of the resected sixth rib. The small diverticulum on the right lateral wall of the middle portion of the esophagus was identified. In the subcarinal area, between the esophagus and the right main bronchus, an oval, almost egg-shaped, mass in the wall of the esophagus was encountered. The mass was relatively large in comparison to the size of the esophagus at this level and measured

approximately 3 by 2 cm. The mass was solid and clearly encroached upon the lumen of the esophagus. A small portion of this tumor was excised for frozen-section microscopic study. The examining pathologist reported that the tissue appeared to be granulomatous rather than neoplastic. The mass had a yellowish appearance on section and was of a firm consistency. It was easily separated from the adjacent normal tissue from which it was sharply demarcated. The mass appeared to have replaced not only the outer muscular layers but a substantial portion of the submucosa and adjacent inner layers as well. The mass was completely removed without entering the lumen of the esophagus. A rather large defect in the wall of the esophagus remained. Throughout the area of this defect, the lumen of the esophagus was covered only by a filmy, tissue-paper thin layer of epithelium and some adjacent lamina propria remnants. It was apparent this defect in the wall of the esophagus, covered as it was only by a thin membrane, could not be left

Fig. 1.—Roentgenogram illustrating esophageal obstruction by extraluminal mass (*dotted line*).

without additional external support. It was feared that approximation of the remaining muscle layers and adjacent submucosa would produce too much constriction in the esophageal lumen at this point. Because of encouraging experience in the laboratory during this period with the use of nylon mesh in the support and repair of experimentally created abdominal wall defects, the use of nylon mesh to support the esophagus in the area of this defect was decided upon.[5] An oval patch of nylon mesh was sutured to the muscle and submucosal layers at the margins of the defect with multiple interrupted sutures of 4-0 silk. The nylon mesh was from the same bolt of material which was used with success in the repair of the abdominal wall defects in the laboratory. It contained 270 by 204 threads per square inch. The thoracotomy incision was closed in layers and a catheter which was left in the chest during closure was aspirated and withdrawn.

On microscopic examination, the tumor was found to be a chronic granulomatous mass with many histiocytes and small numbers of multinucleated giant cells (Fig. 2). Sudan III stain revealed the presence of fat globules in many of the histiocytes. Examination with both the periodic acid-Schiff stain and the Bauer stain failed to reveal the presence of Histoplasma. Tubercle bacilli were not seen.

The patient did well following operation. Gastric suction was maintained for 3 days by means of a nasogastric tube which had been passed into the stomach at the time of operation. Her postoperative course was complicated only by the development of a superficial wound abscess which was satisfactorily managed by drainage. She has experienced no further difficulty with swallowing in the 3 years which have passed since her operation.

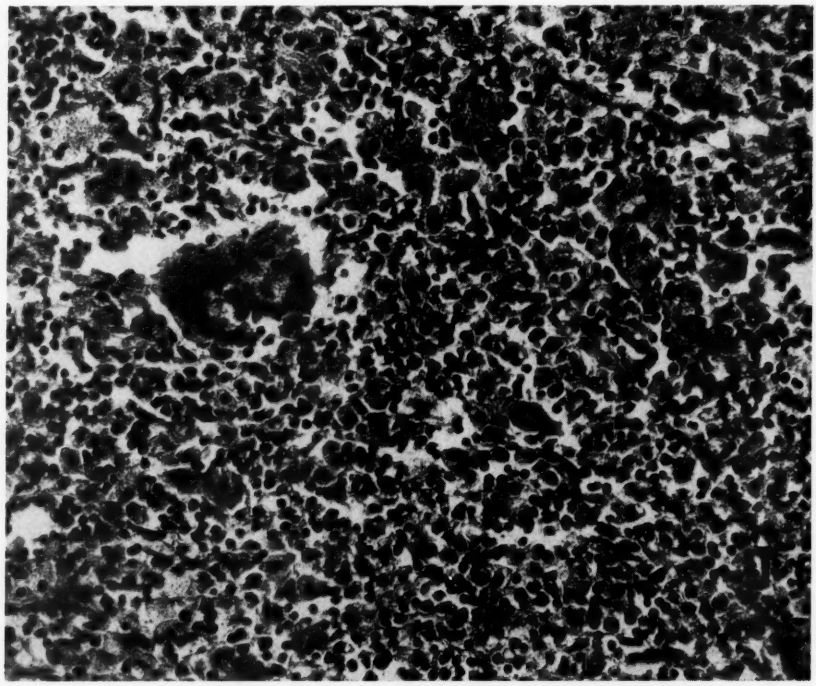

Fig. 2.—Photomicrograph of a section of the resected mass revealing a rather characteristic granulomatous appearance with multinucleated giant cells.

A recent roentgen study of the esophagus with barium, nearly 3 years following operation, showed no evidence of esophageal obstruction, narrowing, or other abnormality. The mucosal pattern of the esophagus appeared to be normal throughout.

Skin testing for sensitivity to tuberculin and histoplasmin was carried out 3 years following operation. The patient was found to have a 4 plus reaction to tuberculin and a 3 plus reaction to histoplasmin.

DISCUSSION

A review of the clinical findings in the 7 recorded cases of surgically managed, symptomatic esophageal obstruction due to mediastinal granuloma, including the case recorded here, reveals that all of the patients were between

the ages of 24 and 43 years (Table I). Five of the 7 patients were females. Dysphagia occurred in all of the patients and was accompanied by chest pain or pain on swallowing in all. The duration of symptoms ranged from 3 weeks to 1 year.

Roentgen study of the esophagus with barium was carried out in 5 patients. In all of them the roentgen studies were interpreted as indicating the presence of an extrinsic, extraluminal mass which was producing esophageal obstruction. Dilatation of the esophagus above the point of obstruction was not observed and the mucosa was found to be intact over the obstructing mass in all 5 cases.

Esophagoscopy was carried out in 4 of the 7 patients. The obstruction was found to be extraluminal and the mucosa intact in all of them. No attempts were made to biopsy the obstructing mass through the intact mucosa. One examination, that reported by Samson and Dugan,[8] was complicated by esophageal perforation and the development of a mediastinitis.

Preoperative skin tests with tuberculin and histoplasmin were obtained in 2 patients. A 1 plus reaction to tuberculin and a 2 plus reaction to histoplasmin were observed in the first case of Garamella and his associates, while both reactions were negative in their third case. In the case recorded here, skin test reaction to tuberculin 3 years following operation was 4 plus and that to histoplasmin was 3 plus. A few acid-fast bacilli could be identified in a smear from the resected granuloma in only 1 of the 5 patients upon whose granulomas this study was carried out. Culture and guinea pig inoculation of material from this granuloma were negative for tuberculosis. Culture and inoculation studies were negative in all 4 of the granulomas investigated by these techniques.

The mediastinal location of the granuloma in these cases with esophageal obstruction is of considerable interest. The granuloma was reported to be subcarinal in 5 of the 7 cases. In 1 case, the mass was found in the posterior superior mediastinum, adherent to the right side of the trachea. It was located between the trachea and the esophagus. In the case report from the Massachusetts General Hospital, the only cited localization of the mass, at the carina, was based on the roentgen study. In 4 of the cases, the mass was reported at operation to be located between the right main bronchus and the esophagus. These findings suggest that a degree of the esophageal obstruction in these cases may have resulted from the trapping of the esophagus, by the expanding granulomatous mass, between the rigid posterior chest wall and the relatively rigid tracheobronchial tree, with its resulting compression. The mediastinal granuloma was subcarinal in 4 of the 39 cases reviewed by Garamella and his associates and esophageal obstruction with dysphagia was found in all 4.

All 7 of the patients were managed by resection of the granuloma and all recovered. In 2 of the patients, reported by Garamella and his associates, an unspecified area of submucosa was left bare by the resection. These muscular defects in the esophagus were stated to have been repaired in both cases. In the case reported by the author, the granuloma had destroyed not only the muscle layer of the esophageal wall but a portion of the submucosa and adjacent

TABLE I. SUMMARY OF REPORTED EXPERIENCE WITH ESOPHAGEAL OBSTRUCTION DUE TO MEDIASTINAL GRANULOMA

CASE NO.	AUTHOR	YEAR	AGE	SEX	SYMPTOMS	DURATION OF SYMPTOMS	MEDIASTINAL LOCATION OF GRANULOMA	OPERATION	RESULT	REMARKS
1.	Case report of Mass. Gen. Hosp.[3] Case 31341	1945	43	F	Dysphagia, pain	6 weeks	At carina	Excision of granuloma	Recovered	Location of mass from roentgen study; anatomic location of mass at operation not given
2.	Samson, et al.[7] Case 1	1950	27	F	Dysphagia, pain	12 months	Right posterior superior	Excision of granuloma	Recovered	Mass adherent to right side of trachea and located between trachea and esophagus
3.	Samson and Dugan.[8] Case 2	1951	29	F	Dysphagia, pain	3 months	Right subcarinal	Excision of granuloma	Recovered	
4.	Garamella, et al.[1] Case 1	1955	24	M	Dysphagia, pain	5 months	Right subcarinal	Excision of granuloma*	Recovered	Mass between right main bronchus and esophagus
5.	Garamella, et al. Case 2	1955	39	F	Dysphagia, pain	10 weeks	Right subcarinal	Excision of granuloma*	Recovered	Mass between right main bronchus and esophagus
6.	Garamella, et al. Case 3	1955	25	M	Dysphagia, pain	3 weeks	Right subcarinal	Excision of granuloma	Recovered	Mass between right main bronchus and esophagus
7.	Moore	1958	43	F	Dysphagia, pain	1 month	Right subcarinal	Excision of granuloma; nylon mesh support of esophageal defect	Recovered	Mass between right main bronchus and esophagus

*Area of submucosa left bare by excision. Muscle defect repaired.

outer mucosal layer as well. Although the granuloma was excised without entering the lumen of the esophagus, the mucosal remnant left covering the esophageal lumen was much too insubstantial to be left without additional support. Because of the size of the defect, it was feared that approximation of the adjacent intact walls of the esophagus would produce too much narrowing of the lumen of the esophagus. The use of a patch of fine-mesh nylon was decided upon to provide the needed support because of the successful experience of the author and Siderys,[5] at this time, with this material in the experimental repair of abdominal wall defects in animals. The nylon patch appeared to have been tolerated well despite the prior presence in the repaired area of a granulomatous mass. Recent experimental studies in dogs have shown nylon mesh patches to be tolerated satisfactorily in the wall of the esophagus.[4]

SUMMARY

1. The literature pertaining to mediastinal granulomas, especially those granulomas which produce symptomatic esophageal obstruction, is reviewed.

2. A case of esophageal obstruction in a 43-year-old woman with increasing dysphagia and pain, due to a subcarinal mediastinal granuloma, is reported. The patient was managed successfully by resection of the granuloma and the use of a patch of fine-mesh nylon for support in the area of resulting esophageal wall weakness.

3. The reported experience in 7 operatively treated cases of symptomatic esophageal obstruction, due to mediastinal granuloma, is analyzed.

4. The dysphagia was found to be accompanied by chest pain or pain on swallowing and these symptoms were often of increasing severity.

5. The mediastinal granulomas which produced symptoms of esophageal obstruction tended to occur most frequently in the subcarinal area. It is surmised that the obstruction in these cases may have resulted from the compressing effect of an expanding granulomatous mass in this relatively unyielding area between the rigid posterior chest wall and the somewhat less rigid, but structurally firm, tracheobronchial tree. Mediastinal granulomas in other areas rarely produced symptoms of esophageal obstruction.

6. The bacteriologic and histologic studies carried out in these cases were of little assistance in establishing the pathogenesis of these granulomas. A more vigorous search for the possible presence of histoplasmosis, by skin testing and special histologic study of the granuloma, is urged in future cases.

7. In patients with symptomatic esophageal obstruction due to an extraluminal mass in the subcarinal area, associated with pain, the diagnosis of mediastinal granuloma should be strongly considered.

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